
From: Lambert, Richard (NIH/NIAID) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9668E9326D084AC893665B084FDFD4FE-LAMBERTR]
Sent: 4/19/2018 10:38:21 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: [Ip-health] KEI sues NIH over license of CD30 CAR T patents to Gilead | Knowledge Ecology International

Sent with BlackBerry Work
(www.blackberry.com)

From: James Love <james.love@keionline.org>
Date: Thursday, Apr 19, 2018, 4:52 PM
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] KEI sues NIH over license of CD30 CAR T patents to Gilead | Knowledge Ecology International

KEI just filed a lawsuit against the NIH. The complaint and the issues in the suit are described here:

<https://www.keionline.org/27669>

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Kleinman, Joe (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A61F3DA68A824FD284D8FD06C81882B7-KLEINMANJ]
Sent: 4/19/2018 2:57:34 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Wyatt, Richard G (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=728cbe2fe91640be9dd1156c9c9f72f4-wyattrg]; Gottesman, Michael (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=918c2344931542a592d00dbe83d3d5a3-gottesmm]; McBurney, Margaret (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=efdfd5476a884ff7bacfb38cb2805863-mmcburney]
Subject: RE: ES - WF 371552 - Clearance (Reviewer)
Attachments: DR01 - Response dft Exondys 51 04172018ah.docx_Clearance_1.pdf

Hi Mark,

This response just came to us for urgent clearance due at 1pm today. Do you have any reservations regarding the reply, or should Richard clear it without delay?

Thanks,

Joe

From: EDRMS_NO_REPLY@mail.nih.gov [mailto:EDRMS_NO_REPLY@mail.nih.gov]
Sent: Thursday, April 19, 2018 10:52 AM
To: Kleinman, Joe (NIH/OD) [E] <joseph.kleinman@nih.gov>; McBurney, Margaret (NIH/OD) [E] <margaret.mcburney@nih.gov>; EDRMS_NO_REPLY (NIH/OD) <EDRMSNOREPLY@od.nih.gov>; Kleinman, Joe (NIH/OD) [E] <joseph.kleinman@nih.gov>; McBurney, Margaret (NIH/OD) [E] <margaret.mcburney@nih.gov>; EDRMS_NO_REPLY (NIH/OD) <EDRMSNOREPLY@od.nih.gov>
Subject: ES - WF 371552 - Clearance (Reviewer)

To whom it may concern:

Message from the Director's Document and Records Management System (DDRMS)

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If you have concerns please contact the NIH Help Desk at (301) 496-4357.

Work Folder Information

Work Folder: WF 371552

Process: Clearance

Program Analyst: Crone, Colleen (NIH/OD) [E]

Due Date: April 19, 2018

WF Subject: OS forwards for direct reply letter from James Love from Knowledge Ecology International (KEI) requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents.

IC: od_oir

From: Love, James

To: Azar, Alex

Remarks: This OER draft direct reply to James Love on behalf of the Secretary is forwarded to NINDS, OIR, OM, OMA,

REL0000023654

OGC, OCPL, OLPA, and OSP for review/clearance. Document for review begins with "DR01." DUE: 04/19/18 1:00 PM.
Apologies for short turnaround; this is due to the OS deadline. Thank you. Colleen

Additional instructions are included on the task form, click the link to open the Task

DRAFT

Mr. James Love
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, D.C. 20009

Sent By Email: james.love@keionline.org

Subject: KEI April 5, 2018 Letter to HHS Secretary Azar on Exondys 51

Dear Mr. Love:

The National Institutes of Health (NIH) is responding to your April 5, 2018 request that was signed by Knowledge Ecology International (KEI) and five other organizations (KEI Request) to Secretary Azar concerning Exondys 51®. The KEI Request asked that Health and Human Services (HHS) exercise its rights under the Bayh-Dole Act to take title to five patents on eteplirsen, as a remedy to a failure by the University of Western Australia to disclose NIH funding of the inventions, and to use the ownership of those patents as leverage to obtain lower prices to Exondys 51®.

NIH is currently reviewing the information KEI provided along with, NIH funding records, disclosures to NIH of any applicable inventions, the U.S. Patent and Trademark Office records, and any other relevant documents. When NIH's analysis is completed we will notify you.

Sincerely,

cc: Health GAP
Patients for Affordable Drugs
People of Faith for Access to Medicines
Social Security Works
Universities Allied for Essential Medicines
HHS OIG - Daniel R. Levinson

REL0000023654.0001

From: Plude, Denise (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=91F83D681D984EAA8FE3DE287AEBFA01-PLUDEDE]
Sent: 4/19/2018 3:17:41 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Dodson, Sara (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=985a956eaa0d4945bdcfd8ea30947d68-dodsonse]
CC: Wertz, Jennifer (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1e6cb9797cef40f1b40e777afe3795d7-wertzj]
Subject: WF 371552 - URGENT due today 1pm
Attachments: 1 Email 00394060 5 4 2018.pdf; 2 Eteplirsen-Exondys-51-cover-letter-5April2018.pdf; 3 Exondys51-Eteplirsen-patents-5April2018.pdf; DR01 - Response dft Exondys 51 04172018ah.docx

Please send your comments ASAP so Lyric has time to review before 1pm

Work Folder Information

Work Folder: WF 371552

Process: Clearance

Program Analyst: Crone, Colleen (NIH/OD) [E]

Due Date: April 19, 2018

WF Subject: OS forwards for direct reply letter from James Love from Knowledge Ecology International (KEI) requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents.

IC: od_osp

From: Love, James

To: Azar, Alex

Remarks: This OER draft direct reply to James Love on behalf of the Secretary is forwarded to NINDS, OIR, OM, OMA, OGC, OCPL, OLPA, and OSP for review/clearance. Document for review begins with "DR01."
DUE: 04/19/18 1:00 PM. Apologies for short turnaround; this is due to the OS deadline. Thank you. Colleen

FW: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51

From: James Love [mailto:james.love@keionline.org]

Sent: Thursday, April 5, 2018 1:18 AM

To: HHS Secretary (HHS/IOS) <secretary@hhs.gov>

Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Levinson, Dan R (OIG/IO) <Dan.Levinson@oig.hhs.gov>; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Kim Treanor <kim.treanor@keionline.org>; Andrew S. Goldman <andrew.goldman@keionline.org>; Manon Ress <manon.ress@keionline.org>

Subject: Letter requesting investigation of and remedy to non-disclosure of NIH funding for 5 patents on Exondys 51

The Honorable Alex Azar

Secretary

Department of Health and Human Services

Via email: secretary@hhs.gov<mailto:secretary@hhs.gov>

Dear Secretary Azar,

Attached is a letter, signed by six organizations, asking for an investigation of and remedy to the failure of inventors to disclose several NIH grants in five patents on the drug Exondys 51. Also attached is a memo providing background on the failure to disclose the NIH grants in the specific patents.

We have requested a meeting with your staff to discuss this issue.

REL0000023655.0001

James Love

Knowledge Ecology International

cc::

The Honorable Daniel R. Levinson,

Dan.Levinson@oig.hhs.gov<mailto:Dan.Levinson@oig.hhs.gov>;

Director Ann Hammersla, hammerslaa@mail.nih.gov<mailto:hammerslaa@mail.nih.gov>

NIH Director Francis.Collins@nih.hhs.gov<mailto:Francis.Collins@nih.hhs.gov>

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

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twitter.com/jamie_love<http://twitter.com/jamie_love>

April 5, 2018

The Honorable Alex Azar
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Via email: secretary@hhs.gov

Re: Using the undisclosed NIH funding for patents on eteplirsen (brand name: Exondys 51) as leverage to lower the price

Dear Secretary Azar:

We are writing to ask the Department of Health and Human Services (HHS) to take action to lower the price of eteplirsen, a drug marketed by Sarepta Therapeutics under the brand name Exondys 51 as a treatment for Duchenne muscular dystrophy (DMD).

Specifically, we are asking that HHS exercise its rights, under the Bayh-Dole Act and contractual agreements with funding agencies, to take title to five patents on eteplirsen, as a remedy to a failure to disclose NIH funding of the inventions, and to use the ownership of those patents as leverage to obtain lower prices.

There is a strong case to be made for changes in legislation to address drug pricing concerns more generally, but even without new legislation, your office has opportunities to address excessive pricing for some products, including Exondys 51, due to the federal government's role in funding the research for the patented inventions.

The mechanism that we highlight in this letter addresses one set of circumstances that give HHS such leverage -- a failure by inventors to disclose federal research funding for patented inventions, which renders them subject to possible sanctions by the funding agency.

In the past, the federal government has, on several occasions, asked recipients of federal grants and contracts to correct failures to disclose federal funding of the inventions, but has not exercised its rights to take the title of such patents for purposes of influencing drug prices. In this respect, we recognize that we are asking HHS to do something new.

The attached memorandum titled, "Undisclosed NIH funding for patents on eteplirsen (brand name: Exondys 51)," identifies five patents that failed to disclose NIH funding, including three patents listed in the FDA Orange Book for Exondys 51. This failure would represent a violation of the Bayh-Dole Act, attendant regulations, and HHS guidance.

Exondys 51 is expensive. The annual cost of treatment is \$750,000 to \$1.5 million for some patients. As was reported in a moving 2017 article and video published in the New York Times, the high price has limited access to the treatment.¹

The development of Exondys 51 has been subsidized by research grants provided by the National Institutes of Health, charities, and governments in Europe and Australia, including eight NIH-funded projects awarded to the University of Western Australia (UWA) and several NIH funded projects where Patrick Iversen (a Sarepta affiliated researcher) was the principal investigator. In addition, Sarepta has benefited from a variety of other federal government subsidies, including grants from the federal government's Qualifying Therapeutic Discovery Project (QTDP) program, the Orphan Drug Tax Credit, and a priority review voucher which Sarepta sold to Gilead for \$125 million. In addition, the European Commission, the UK government, and other government research agencies have funded key elements of the development of this drug.

The key trial used to approve Exondys 51 only involved 12 patients. The small size of the pre-approval trials, combined with the significant public sector research grants, tax credits and subsidies for development of the drug, as well as the award of a priority review voucher, are relevant to evaluating the need to address the excessive price.

Exondys 51 has orphan drug exclusivity until September 19, 2023, and there are two patents in the FDA Orange Book for which we have not identified federal funding. However, because several patents did have NIH funding and failed to disclose such funding, HHS has leverage it can exercise if willing to do so.

As the Secretary of HHS, you have the authority to take title to at least five of Exondys 51's patents as a remedy for the failure to disclose federal funding in the inventions.

If HHS obtains title to the five patents, it can at a minimum seek damages for infringement of the patents. HHS is also in a negotiating position to facilitate earlier competition, both in the United States² and in the European Union³, and Sarepta must consider these potential consequences.

In the past, the NIH has asked grant recipients to correct the disclosures, but normally has not sought to impose sanctions for the past failures, such as taking title to the patents, despite a

¹ Katie Thomas, [Insurers Battle Families Over Costly Drug for Fatal Disease](#), *New York Times*, June 22, 2017.

² For the U.S. market, the government could use 28 USC § 1498 to overcome any patents that do not have established rights pursuant to the Bayh-Dole Act, because the compensation for that patent would be considerably less if the United States retained title to or held a royalty-free right in the other NIH-funded eteplirsen patents.

³ The U.S. could make a credible threat to shorten the monopoly in Europe, where orphan drug exclusivity can be revoked after six years upon a showing that the incentive was not necessary, and where governments in Europe may have similar rights a patent assigned to Academisch Ziekenhuis Leiden, in the Netherlands. See also, REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 1999 on orphan medicinal products. Article 8. Market exclusivity. "2. This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the medicinal product concerned, that the criteria laid down in Article 3 are no longer met, inter alia, where it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity."

history of unfortunate non-compliance by grant recipients.⁴ Clearly we are asking for HHS to take stronger measures in this case. Given the orphan drug exclusivity for Exondys 51, the stronger measures are necessary for HHS to have leverage to lower the excessive and access-restricting price.

We respectfully ask for a meeting with your staff to further discuss this issue, noting that as a practical matter, if the decisions are delegated solely to the NIH OTT staff it is highly unlikely any action will be taken to moderate the price of this drug.

Sincerely,

Health GAP
Knowledge Ecology International
Patients for Affordable Drugs
People of Faith for Access to Medicines
Social Security Works
Universities Allied for Essential Medicines

Cc: The Honorable Daniel R. Levinson, Dan.Levinson@oig.hhs.gov; Director Ann Hammersla, hammerslaa@mail.nih.gov

⁴ See, for example: United States General Accounting Office. Technology Transfer Reporting Requirements for Federally Sponsored Inventions Need Revision. Report to the Chairman, Committee on the Judiciary, U.S. Senate. GAO/RCED-99-242. August 1999.

Undisclosed NIH funding for patents on eteplirsen (brand name: Exondys 51)

April 5, 2018

Table of Contents

Introduction	2
Sarepta Therapeutics	3
What does eteplirsen do?	4
Controversy over the FDA approval of Exondys 51	5
The high price of Exondys 51 is a barrier to access	6
Exondys 51 sales	7
Table 1: Exondys 51 sales	7
The FDA Orange Book patents on Exondys 51	8
Table 2: FDA Orange Book patents on Exondys 51	8
Table 3: Patents for eteplirsen listed in the Sarepta Therapeutics 10-K	8
Wilton, Fletcher and McClorey patents that failed to disclose federal funding	9
Table 4: Four Wilton et al. patents for antisense oligonucleotides for inducing exon skipping that failed to disclose NIH grants	9
The related and undisclosed research grants from National Institute of Health	9
Table 5: The NIH grants for antisense oligonucleotides	9
The abstracts for the antisense oligonucleotide grants	10
The Iversen patent that did not disclose federal funding	12
Table 6: Four relevant Iversen projects funded by the NIH from 1997 to 2000	12
The 2006 Nature paper	14
The 2010 QTDP grants	14
Note on extent of disclosures for other patents assigned to Sarepta Therapeutics	14
Remedies for non-disclosure of the eteplirsen patents	15
Attachments	15
Annex 1: Foreign government funding of research	16

Annex 2: Sarepta Therapeutics sale of priority review voucher for Exondys 51	17
Annex 3: Excerpts from the license agreement between the University of Western Australia and Sarepta Therapeutics	17
Annex 4: Patents assigned to Antivirals, Inc., AVI BioPharma or Sarepta Therapeutics which either declare government funding or share an assignment to a U.S. government agency	19
Annex 5: Patents assigned to Antivirals, Inc., AVI BioPharma or Sarepta Therapeutics with no disclosures of federal funding	20
Annex 6: Selected exhibits of Sarepta Therapeutics SEC filings	23

Introduction

Knowledge Ecology International (KEI) has discovered what appears to be a failure to disclose National Institutes of Health (NIH) research funding on four patents granted to Stephen Wilton, Sue Fletcher and Graham McClorey, assigned to the University of Western Australia. The four patents have the same inventors, the same title and the same priority date (June 28, 2004). Two of the four Wilton *et al.* patents are listed in the FDA Orange Book for the drug marketed by Sarepta Therapeutics as Exondys 51 (INN eteplirsen), a treatment for Duchenne Muscular Dystrophy (DMD).

From 2004 to 2012, Stephen Wilton was the principal investigator for eight projects awarded \$1,508,360 in total funding by the U.S. NIH, National Institute of Neurological Disorders and Stroke (NINDS) for research on antisense oligonucleotides and Duchenne muscular dystrophy (DMD). The grants were directly related to the four Wilton *et al.* patents.

KEI has also determined there was a failure to disclose federal research funding for patent 9,416,361, which lists Patrick Iversen and Robert Hudziak as inventors, and is assigned to Sarepta Therapeutics. This patent is also listed in the FDA Orange Book for Exondys 51.

The Sarepta price for Exondys 51 is excessive, and the high cost has created significant access barriers and hardships for patients. According to one analyst who reviewed insurance claims, the annual cost of the treatment for some patients will be in the range of \$750,000 to \$1.5 million, which does not include other drugs that may be required for treatment.¹

¹ Katie Thomas, [Insurers Battle Families Over Costly Drug for Fatal Disease](#), *New York Times*. June 22, 2017.

Not all of the patents listed in the FDA Orange Book have identified U.S. government funding, and the drug is protected by the U.S. orphan drug exclusivity through September 19, 2023. However, the failure by inventors to disclose NIH funding provides the United States government with an opportunity to take title to at least five relevant Exondys 51 patents, and to use the ownership of the patents as leverage to lower the price.

KEI also suggests that the NIH and the U.S. Department of Defense review 91 other patents assigned to Sarepta which do not disclose federal research funding.

Finally, this case illustrates an area for potential future cooperation between the United States and other governments, as regards government rights in patents. One patent in the Orange Book for Exondys 51 is assigned to the Academisch Ziekenhuis Leiden in the Netherlands, an institution that receives research funding from the Dutch government and the European Union. The University of Western Australia also claimed DMD-related funding from the Western Australia Medical and Health Research Infrastructure Fund (MHRIF). An agreement among governments on the financing of biomedical R&D (as has been proposed for the World Health Organization), could include provisions for cross-licensing government rights in patents.

Sarepta Therapeutics

Sarepta Therapeutics is the current name of the firm first known as AntiVirals, Inc. and later as Avi BioPharma.

AntiVirals, Inc. was incorporated in the state of Oregon on July 22, 1980 to develop and commercialize therapeutic products based upon antisense and cancer immunotherapy technology. In 2002, the company was renamed Avi BioPharma. In July 2009, the company moved its headquarters from Portland, Oregon to Bothell, Washington.²

In 2012, the company changed its name to Sarepta Therapeutics and moved to Cambridge, Massachusetts, motivated by the need to recruit expertise in rare diseases.³

Over time, the company expanded its focus and explored other areas of research, funded through a variety of sources including stock sales, collaborations and government grants and contracts.

² Luke Timmerman, [AVI Biopharma Bolts from Portland to Seattle to Tap Biotech Talent](#), *Xconomy*. July 30, 2009.

³ Luke Timmerman, [Sarepta Moves From Seattle to Boston for the Talent](#), *Xconomy*. September 7, 2012; Don Seiffer, [Here's why Sarepta Therapeutics is consolidating in Massachusetts](#), *Boston Business Journal*. March 9, 2016.

At one point nearly all of the firm's revenue was based upon government contracts and grants, primarily from Department of Defense and the NIH, relating to research on a variety of infectious diseases and on Duchenne muscular dystrophy (DMD).

In 2011, several large research contracts from the Department of Defense began to wind down.

What does eteplirsen do?

Eteplirsen, once named AVI-4658, is a drug sold by Sarepta Therapeutics under the trade name Exondys 51 for the treatment of Duchenne muscular dystrophy (DMD).

The FDA approved the sale of Exondys 51 on September 19, 2016. The FDA press release about the approval offered this description:⁴

The U.S. Food and Drug Administration today approved Exondys 51 (eteplirsen) injection, the first drug approved to treat patients with Duchenne muscular dystrophy (DMD). Exondys 51 is specifically indicated for patients who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13 percent of the population with DMD. . .

DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. It is the most common type of muscular dystrophy. DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. The first symptoms are usually seen between three and five years of age, and worsen over time. The disease often occurs in people without a known family history of the condition and primarily affects boys, but in rare cases it can affect girls. DMD occurs in about one out of every 3,600 male infants worldwide.

People with DMD progressively lose the ability to perform activities independently and often require use of a wheelchair by their early teens. As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.

Katie Thomas, writing for the New York Times, said:⁵

“Exondys 51 may be helping protect muscle cells from deterioration by producing a form of dystrophin, a protein largely lacking in those with the genetic mutation. The

⁴ FDA Press Release, [FDA grants accelerated approval to first drug for Duchenne muscular dystrophy](#), September 19, 2016.

⁵ Katie Thomas, [Insurers Battle Families Over Costly Drug for Fatal Disease](#), *New York Times*. June 22, 2017.

boys typically need wheelchairs by their teenage years, and their hearts and lungs eventually give out. Between 9,000 and 12,000 people are estimated to be living with Duchenne in the United States; about 13 percent have the genetic mutation receptive to the new drug.”

Controversy over the FDA approval of Exondys 51

The approval of Exondys 51 was controversial because of the small number of the patients in the clinical trials, and because a review panel had narrowly recommended against the approval before being overruled by FDA Commissioner Dr. Janet Woodcock.

Below are some of the commentary regarding the approval of Exondys 51.

Editorial, “Railroading at the FDA,” *Nature Medicine*. Vol. 22, Num. 1193 (2016).
[doi:10.1038/nm.4234](https://doi.org/10.1038/nm.4234)

“In the words of one FDA committee member, Exondys lowers the agency's evidentiary standard for drug effectiveness ‘to an unprecedented nadir.’”

Sy Mukherjee, “[The FDA Just Made Its Most Controversial Drug Approval of the Year](#),” *Fortune*. September 19, 2016.

“What’s striking about the FDA approval is that it overrules its own scientific advisers. An independent advisory panel voted against recommending approval in a highly polarized 7-6 vote in April, adding that the company’s clinical trials for the treatment were poorly designed. But Sarepta had two key allies on its side that buttressed the biotech’s chances and led to Monday’s reversal: the DMD patient community, which flooded the ill-fated April FDA panel meeting on the therapy with highly personal, heart-wrenching testimony, and Dr. Janet Woodcock, the director of the FDA’s Center for Drug Evaluation and Research (CDER).”

John Carroll, “[FDA officials: There was “no scientific basis” for Duchenne drug OK as Sarepta complained of “dire financial” condition](#),” *Endpoints News*. November 4, 2016.

“Two senior FDA officials mounted a vehement assault on Janet Woodcock’s decision to push through an approval of Sarepta’s Duchenne muscular dystrophy drug Exondys 51. New documents posted by the FDA, including a round of memos on the issue in September, warned FDA Commissioner Robert Califf that he was allowing an approval even though Woodcock had not considered all the analysis they had done to underscore the company’s weak case, adding that there was no scientific basis to conclude that the drug was reasonably likely to benefit patients.”

The high price of Exondys 51 is a barrier to access

After the approval of Exondys 51, the editors of *BIOCentury* defended the accelerated approval but expressed concern over the price:⁶

“We still believe accelerated approval was the right decision. Unfortunately, judging by the \$300,000 annual net cost for a drug that at this point is only “reasonably likely” to produce a clinical benefit, it looks like Sarepta is continuing to get it wrong. Unless the company engages in risk-sharing or pay-for-performance deals with payers, the high price will prevent broad access to the drug -- and giving patients broad access was the best reason to grant this drug accelerated approval.”

It appears, however, that the costs are far higher than \$300,000 per year.

This drug, administered once weekly, is available either in a 2 ml or 10 ml vial depending on the weight of the patient. The 2 ml vial costs \$1,600 whilst the 10 ml vial costs \$8,000.

The 2017 article by Katie Thomas in the New York Times reported that an analysis by Prime Therapeutics estimated the average cost of the drug, at its list price, for the twelve patients in the main clinical trial cited by the FDA when the drug was approved, at \$750,000 each, more than double the \$300,000 per child figure announced by the manufacturer.⁷

“I’m reading a lot of denial letters,” said Christine McSherry, who until recently served as executive director of the Jett Foundation, an advocacy group that guides families through the insurance appeal process. Her insurer, Blue Cross Blue Shield of Massachusetts, is covering the drug for her son, Jett, through next April. “It’s very disheartening to have worked that hard, and to have sacrificed that much, and to now have to battle the insurance companies.”

The drug’s high cost is driving the resistance. While the drug manufacturer, Sarepta, has said Exondys 51 costs about \$300,000 a year per child, the price, based on a child’s weight, can be much higher. For the dozen boys in the main clinical trial, the average list price would be more than double Sarepta’s quote — \$750,000 each, according to an analysis by the drug benefit firm Prime Therapeutics.

⁶ Susan Schaeffer (Editor, *BioCentury*), Erin Mccallister (Senior Editor), And Steve Usdin (Washington Editor), Wrong Again: Why Sarepta’s \$300k Price For Dmd Drug Invalidates Reasons For Accelerated Approval, *BioCentury*. September 26, 2016.

⁷ Katie Thomas, Insurers Battle Families Over Costly Drug for Fatal Disease, *New York Times*. June 22, 2017.

Thomas reported that for some patients, the cost is as high as \$1.5 million per year, or more than \$4,000 per day, and that patients are concerned that the treatment will also require the use of other expensive drugs.⁸

Sarepta's executives have claimed in statements that the average price for Exondys 51 is \$300,000 per patient per year.

"That's not accurate," said David Lassen, the chief clinical officer at Prime Therapeutics, which manages the drug plans for more than 20 million Americans. "Based on just the few claims that we've evaluated, we think that's low." He cited a range from \$750,000 to \$1.5 million a year, far greater than breakthrough drugs like, for instance, cystic fibrosis treatments sold by Vertex that cost more than \$250,000 a year.

Sarepta contends that the \$300,000 estimate is a net price, accounting for discounts to insurers and the fact that not everyone will follow the weekly regimen. It also includes the assumption that younger boys who weigh less will begin taking the drug.

"What we have seen is that for some of the older, sicker boys who have been using it, the price is more," said Dr. Ed Kaye, the chief executive of Sarepta.

Many Duchenne parents worry that insurers will balk if other costly drugs are approved to complement the treatment from Exondys 51. Already, they are reeling from the decision by PTC Therapeutics to price a once-cheap steroid, deflazacort, at about \$35,000 per year. Many families had been importing it for about \$1,600 a year.

Exondys 51 sales

Exondys 51 was approved for sale on September 19, 2016. Net sales from product sales are as follows:

Table 1: Exondys 51 sales

Period	Sales
2016	\$ 5,421
2017:Q1	\$16,340
2017:Q2	\$35,011
2017:Q3	\$45,954
2017:Q4	\$57,277

⁸ *Ibid.*

The FDA Orange Book patents on Exondys 51

On March 14, 2018, there were five patents listed in the Orange Book for Exondys 51. Two were assigned to the University of Western Australia, two were assigned to Sarepta Therapeutics in Cambridge, Massachusetts, and one jointly to an academic institution and a biomedical company both in Leiden, Netherlands.

Table 2: FDA Orange Book patents on Exondys 51

Patent Number	File date	Grant date	Priority Date	Expiration	Inventors	Assignee
8486907	Oct 11 2011	Jul 16 2013	Jun 28, 2004 [AU]	Jun 28 2025	Wilton; Stephen Donald (Applecross, AU), Fletcher; Sue (Bayswater, AU), McClorey; Graham (Bayswater, AU)	The University of Western Australia
9018368	Jun 26 2014	Apr 28 2015	Jun 28, 2004 [AU]	Jun 28 2025	Wilton; Stephen Donald (Applecross, AU), Fletcher; Sue (Bayswater, AU), McClorey; Graham (Bayswater, AU)	The University of Western Australia
9243245	Apr 26 2010	Jan 26 2016	Oct 26, 2007 [EP]	Oct 27, 2028	De Kimpe; Josephus Johannes (Utrecht, NL), Platenburg; Gerard Johannes (Voorschoten, NL), Van Deutekom; Judith Christina Theodora (Dordrecht, NL), Aartsma-Rus; Annemieke (Hoofddorp, NL), Van Ommen; Garrit-Jan Boudewijn (Amsterdam, NL)	Academisch Ziekenhuis Leiden (Leiden, NL), BioMarin Technologies B.V. (Leiden, NL)
9416361	Nov 6 2014	Aug 16 2016	May 4 2000	May 4, 2021	Iversen; Patrick L. (Corvallis, OR), Hudziak; Robert (Blodgett, OR)	Sarepta Therapeutics, Inc.
9506058	Mar 14 2014	11/29/ 2016	Mar 15 2013	Mar 14, 2034	Kaye; Edward M. (Cambridge, MA)	Sarepta Therapeutics, Inc.

The 2017 Sarepta Therapeutics Securities and Exchange Commission (SEC) 10-K annual report lists seven patents for eteplirsen (Exondys 51), including two earlier patents (7,807,816 and 7,960,541) assigned to the University of Western Australia that are currently not listed in the FDA Orange Book. The two earlier UWA patents have the same inventors, title and priority date as the two newer UWA ones.

Table 3: Patents for *eteplirsen* listed in the Sarepta Therapeutics 10-K

Patent	Type	Expiration	Owner
7,807,816	Composition of Matter	February 23, 2026	UWA
7,960,541	Composition of Matter	June 28, 2025	UWA
8,486,907	Methods of Use	June 28, 2025	UWA
9,018,368	Composition of Matter	June 28, 2025	UWA
9,243,245	Methods of Use	October 27, 2028	BioMarin/AZL
9,416,361	Composition of Matter	May 4, 2021	Sarepta
9,506,058	Methods of Use	March 14, 2034	Sarepta

Wilton, Fletcher and McClorey patents that failed to disclose federal funding

The four patents assigned to the University of Western Australia for antisense oligonucleotides for inducing exon skipping are listed in Table 4.

Table 4: Four Wilton *et al.* patents for antisense oligonucleotides for inducing exon skipping that failed to disclose NIH grants

Patent number	Date filed	Date granted	Priority date	Title
7,807,816	01/05/2006	10/05/2010	6/28/2004	Antisense oligonucleotides for inducing exon skipping and methods of use thereof
7,960,541	8/20/2010	6/14/2011	6/28/2004	Antisense oligonucleotides for inducing exon skipping and methods of use thereof
8,486,907	10/11/2011	7/16/2013	6/28/2004	Antisense oligonucleotides for inducing exon skipping and methods of use thereof
9,018,368	6/26/2014	4/28/2015	6/28/2004	Antisense oligonucleotides for inducing exon skipping and methods of use thereof

The patents in Table 4 have different filing and grant dates, but the exact same title and the same priority date of June 28, 2004.

The related and undisclosed research grants from National Institute of Health

According to the National Institutes of Health RePORTER database, Stephen Wilton was the principal investigator for eight NIH funded projects awarded to the University of Western Australia, involving \$1,508,360. The projects were from the National Institute of Neurological Disorders and Stroke (NINDS), for fiscal years 2004 to 2012.

Table 5: The NIH grants for antisense oligonucleotides

Grant number	Title	PI	Budget Start Date	Budget End Date	Agency
5 R01 NS044146 01A2	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF DMD</u>	WILTON, STEPHEN D	1/1/04	12/1/04	NINDS
5 R01 NS044146 02	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF DMD</u>	WILTON, STEPHEN D	1/1/05	12/31/05	NINDS
5 R01 NS044146 03	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF DMD</u>	WILTON, STEPHEN D	1/1/06	12/31/06	NINDS

KEI Series on patents that fail to disclose U.S. government funding

5 R01 NS044146 04	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF DUCHENNE MUSCULAR DYSTROPHY</u>	WILTON, STEPHEN D	1/1/07	12/31/07	NINDS
5 R01 NS044146 05A1	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF NON-DELETION DMD CAUSING MUTATIONS</u>	WILTON, STEPHEN D	4/15/09	3/31/10	NINDS
5 R01 NS044146 06	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF NON-DELETION DMD CAUSING MUTATIONS</u>	WILTON, STEPHEN D	4/1/10	3/31/11	NINDS
5 R01 NS044146 07	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF NON-DELETION DMD CAUSING MUTATIONS</u>	WILTON, STEPHEN D	1-Apr-2011	3/31/12	NINDS
5 R01 NS044146 08	<u>ANTISENSE OLIGONUCLEOTIDE SUPPRESSION OF NON-DELETION DMD CAUSING MUTATIONS</u>	WILTON, STEPHEN D	4/1/12	3/31/13	NINDS

The titles of all eight projects mention antisense oligonucleotides, a form of technology whereby a sequence complementary to a specific mRNA is used to inhibit expression and prevent the transfer of genetic information from DNA to protein, for the treatment of Duchenne Muscular Dystrophy (DMD).

The abstracts given for the grants are as follows:

The abstracts for the antisense oligonucleotide grants

5 R01 NS044146 01A2, 5 R01 NS044146 02, 5 R01 NS044146 03 and 5 R01 NS044146 04

DESCRIPTION (provided by applicant): The ultimate goal of this project is to develop an antisense oligonucleotide (AO) therapy for Duchenne muscular dystrophy (DMD). Antisense oligonucleotides (AOs) can be used to reduce the severity of DMD by removing specific exons during pre-mRNA splicing, to either by-pass nonsense mutations or restore the reading frame around dystrophin genomic deletions. As a result of the treatment, dystrophin expression would be restored in dystrophic tissue and DMD patients would theoretically manifest only the milder phenotype of Becker Muscular Dystrophy (BMD). This project will explore the design and delivery of AOs to minimize the consequences of disease-causing dystrophin gene mutations. (1) Animal models of muscular dystrophy will be used to develop treatment regimens and assess therapeutic benefits in vivo. (2) AOs will be designed to target the most amenable splicing motifs at relevant exons in the human dystrophin gene transcript and will be evaluated in cultured human muscle cells. Although this approach cannot permanently correct the primary genetic lesion, we propose that repeated administration, preferably through systemic delivery, should be feasible. AO chemistries or modifications to increase stability and/or uptake, optimized for in vivo induction of exon skipping, will be developed and evaluated. Only periodic administration of AOs should be required to maintain therapeutic levels of induced dystrophin in dystrophic muscle. DMD is a serious disorder for which there is no effective treatment. AOs will not cure this devastating condition, however, AO-based splicing intervention has the potential to reduce the severity of DMD so that treated boys should be able to produce some functional dystrophin. This would be expected to moderate the severity of DMD and improve the quality of life for patients and their families.

5 R01 NS044146 05A1, 5 R01 NS044146 06, 5 R01 NS044146 07 and 5 R01 NS044146 08

DESCRIPTION (provided by applicant): Duchenne muscular dystrophy (DMD) is a fatal X-linked muscle-wasting disorder caused by protein truncating mutations in the dystrophin gene. Antisense oligomer induced removal of an exon carrying a nonsense mutation, or exons flanking frame-shifting deletions, the most common type of DMD mutation, has been shown to generate an in-frame message and an internally deleted, but functional protein. Becker muscular dystrophy (BMD) is an allelic disorder typically caused by in-frame deletions of one or more exons, most commonly in the first two thirds of the gene. The severity of BMD varies from borderline DMD to asymptomatic, and the dystrophin genes in mildly affected BMD patients provide an indication of functional exon combinations. At least one third of DMD cases result from duplications, micro-insertions/deletions and single base changes that alter splice site recognition or cause premature termination of translation. This project will address the design and application of antisense oligomers for induced exon skipping, for those DMD cases caused by non-deletion mutations. Patient cell lines will be transfected with test compounds and exon skipping assessed. Exon skipping strategies will be modified to maximize induced dystrophin quality and quantity, as permitted by the context of each particular dystrophin gene lesion. The specific aims are to: 7 Optimise antisense oligomers to remove exons carrying sequence variations (disease-causing or neutral polymorphisms) that would otherwise compromise exon skipping. 7 Develop exon skipping strategies appropriate to DMD cases caused by pseudo-exon incorporation or duplications of one or more exons. 7 Develop transient animal models to identify functionally significant dystrophin domains, according to exon boundaries, to facilitate design of optimal exon skipping strategies. PUBLIC HEALTH RELEVANCE: Duchenne muscular dystrophy is a relentlessly progressive, fatal disease for which there is no effective treatment. Specific exon removal has the potential to greatly reduce the severity of DMD, and restoration of dystrophin expression, even of partial function in a DMD patient is expected to result in a BMD-like phenotype, and reduce morbidity and extend life expectancy. This application seeks to develop personalised exon skipping therapies for the one third of DMD patients who have non-deletion mutations. Exon skipping should be made available to all patients who could benefit, not only those with the more common exon deletion mutations.

All the patents listed above in Table 4 provide several key terms/words that appear to be the subject matter of the grants, including, to mention a few:

- Antisense Oligonucleotide (ABSTRACT)
- **Exon Skipping** (ABSTRACT)
- Dystrophin gene (ABSTRACT)
- Claim 29 - The method of claim 25, wherein the subject is a human and the muscular dystrophy is **Duchenne muscular dystrophy**. (PAGE 138, PATENT 8,486,907)
- Claim 28 - The method of claim 25, wherein the subject is a human and the muscular dystrophy is **Becker muscular dystrophy**. (PAGE 138, PATENT 8,486,907)
- These **Duchenne muscular dystrophy** gene defects are typically nonsense mutations or genomic rearrangements such as **deletions, duplications or micro-deletions or insertions** that disrupt the reading frame. (PAGE 23, PATENT 8,486,907)
- The acceptor and donor **splice sites** have consensus sequences of about 16 and 8 bases respectively (PAGE 4, PATENT 8,486,907)
- FIG. 2. Diagrammatic representation of the concept of antisense oligonucleotide induced **exon skipping** to by-pass disease-causing mutations (not drawn to scale). The hatched box represents an exon carrying a mutation that prevents the **translation** of the rest of the **mRNA** into a protein. The solid black bar represents an **antisense**

oligonucleotide that prevents inclusion of that **exon** in the mature **mRNA**. (PAGE 5, PATENT 9,018,368)

In 2008, the University of Western Australia licensed its patent rights to Avi BioPharma.

University of Western Australia

In November 2008, we entered into an exclusive license with the University of Western Australia, or UWA, for certain patents and technical information relating to the use of certain antisense sequences for the treatment of DMD. The license grants us specific rights to the treatment of DMD by inducing the skipping of certain exons defined in the agreement.⁹

The Iversen patent that did not disclose federal funding

KEI has discovered that the one patent assigned to Sarepta Therapeutics for Exondys 51 also appears to have failed to report federal funding.

Patent number: 9,416,361

Title: Splice-region antisense composition and method
Inventors: Iversen; Patrick L. (Corvallis, OR), Hudziak; Robert (Blodgett, OR)
Filed: November 6, 2014
Granted: August 16, 2016
Priority: May 4, 2000
Assignee: Sarepta Therapeutics, Inc. (Cambridge, MA)

The NIH funded a series of research projects relevant to this invention from June 1997 to March 31, 2001, a period which spans from before to right after the priority date of the invention. The title of each project was, "Gene Expression Modulators To Control Drug Metabolism." Patrick Iversen was listed as the principal investigator. The first project was a grant to the University of Nebraska Medical Center, and the last three were to Oregon State University.

Table 6: Four relevant Iversen projects funded by the NIH from 1997 to 2000

Fy	Project number	PI	Receipteint	Cost in FY
1997	1R01GM054871-01A1	Iversen, Patrick L.	University Of Nebraska Medical Center	169,248
1998	7R01GM054871-02	Iversen, Patrick L.	Oregon State University	\$114,280

⁹ <https://www.sec.gov/Archives/edgar/data/873303/000119312511066190/d10k.htm>

KEI Series on patents that fail to disclose U.S. government funding

1999	5R01GM054871-03	Iversen, Patrick L.	Oregon State University	\$106,765
2000	5R01GM054871-04	Iversen, Patrick L.	Oregon State University	\$110,076

The abstracts were the same for all four projects and were as follows:

DESCRIPTION (Adapted from Investigator's Abstract): The purpose of this proposal is to exploit the potential for gene-specific activities of synthetic **oligonucleotides** (ODNs) in an animal model involving drug metabolism. The mechanistic actions of nuclease resistant ODNs include sequence-specific interactions with nucleic acids as antigene or antisense molecules or with transcriptional regulatory proteins in a manner that mimics the genomic cis-elements resulting in the modulation of gene expression. The investigators intend to test the hypothesis that optimal **oligonucleotide** structures can be identified that modulate the expression of cytochrome P450 isoforms in vivo. Further, that gene expression modulation will provide insights into the regulation of these genes' expression and their reliance on endogenous substrates and extrahepatic expression. **In vivo** studies are proposed because ODN entry into and distribution within the cell is not equivalent between studies conducted in cultured cells and that observed in intact animals. The specific aims of these studies are to: 1) identify optimal **oligonucleotide** structures for **antisense**, antigene, ribozyme and transcriptional regulation of gene expression in vivo, 2) evaluate the mechanism of action of these modulators of gene expression, 3) identify in **in vivo** modulators a broad spectrum of phase I drug metabolizing enzymes including rat CYP1A1, CYP2B1, CYP2B2, CYP2C11, CYP2E1, **CYP3A2** and CYP4A1 and 4) evaluate these gene expression modulators in context dependent expression created by sex hormones, circadian rhythm, xenobiotic exposure and extrahepatic organs. The advantages of this model system are that 1) constitutive gene expression is monitored in the absence of disease, 2) the in vivo efficacy is confirmed by **in vitro** analysis of enzyme activities and protein levels directly link the target **mRNA** with observed phenotype, 3) toxicity can be evaluated concomitantly with efficacy, 4) the approach is cost effective, 5) this approach avoids discrepancies that are in cell culture and 6) direct comparison of potency, efficacy and toxicity can be made with linear **phosphorothioate** ODNs. Future studies will involve a more detailed investigation of the role of cytochrome P450 expression in the regulation of radical oxygen sensitive genes in vivo.

The descriptions of the invention in the Iversen patent 9,416,361 include several references which are related to the abstract of the grant. For example, from the text of the patent:

- The **antisense** compound is RNase-inactive, and is preferably a **phosphorodiamidate**-linked morpholino **oligonucleotide**.
- A morpholino **antisense oligonucleotide** composition may be administered in any convenient physiologically acceptable vehicle.
- studies were carried out with rat **CYP3A2** pre-mRNA targeted **in vivo** (whole animal). Animals were injected i.p. with 100 .mu.g PMO (as shown in FIG. 3, where Y.sub.1 and Z are oxygen and X is N(CH.sub.3).sub.2) in phosphate buffered saline. The diminished rate of microsomal metabolism of erythromycin O-demethylase was monitored to reflect the expected phenotype caused by the **antisense** inhibition.

Iversen is also listed as the PI for eight other NIH-funded projects, including three grants to Avi Biopharma, which received at least ten NIH-funded projects.

The 2006 Nature paper

In 2005, the three Australian inventors, Iversen, and Hong Moulton (another researcher for Avi BioPharma) co-authored a paper that was published by *Nature* in 2006, with the title, "Antisense oligonucleotide-induced exon skipping restores dystrophin expression in vitro in a canine model of Duchenne muscular dystrophy (DMD)." ¹⁰

The acknowledgements section in the Nature paper states:

"This work was funded by Parent Project Muscular Dystrophy, USA, National Institute of Health, USA, National Health and Medical Research Council, Australia, Muscular Dystrophy Association, USA and the Medical and Health Research Infrastructure Fund, Western Australia."

The 2010 QTDP grants

The Avi BioPharma SEC 10-K report for the fiscal year ended December 31, 2010 reported that the company received five grants from the federal government's Qualifying Therapeutic Discovery Project, or QTDP program, "for our DMD program and infectious disease programs" and that the grant for each application was approximately \$244,000. ¹¹

According to the 10-K report, "the QTDP was part of the March 2010 Patient Protection and Affordable Care Act and provides a tax credit or grant equal to 50 percent of eligible costs and expenses for tax years 2009 and 2010."

Note on extent of disclosures for other patents assigned to Sarepta Therapeutics

We ran two queries of the US Patent & Trademark Office Patent Full Text and Image Database to determine the number of patents assigned to Sarepta Therapeutics in total, and among those patents, the number that disclosed federal funding of the invention.

The first query was:

AN/antivirals OR AN/"avi biopharma" OR AN/sarepta

¹⁰ G McClorey, H M Moulton, P L Iversen, S Fletcher & S D Wilton, Antisense oligonucleotide-induced exon skipping restores dystrophin expression in vitro in a canine model of DMD, *Gene Therapy* volume 13, pages 1373–1381 (2006); doi:10.1038/sj.gt.3302800

¹¹ <https://www.sec.gov/Archives/edgar/data/8733303/000119312511066190/d10k.htm>

Which identified 101 granted patents that were assigned to either “Antivirals” (the original name of the company), “Avi BioPharma” (the second name) or “Sarepta” (the current name).

The second query searched within those 101 identified patents for either a declaration of federal funding, or an assignment to the United States government, the Department of Defense, the Department of Health and Human Services, or the U.S. Army.

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(AN/antivirals OR AN/"avi biopharma" OR AN/sarepta) AND  
(GOVT/government OR AN/defense OR AN/army OR AN/united OR  
AN/health)
```

The second query identified ten of the Antivirals/Avi BioPharma/Sarepta patents that matched criteria, including four patents that disclosed grants (two each from HHS and DoD) and six patents with joint assignments to a federal agency, of which three were jointly assigned with HHS and three others with the U.S. Army.

A list of the patents with and without disclosures or assignments to a federal agency are provided in Annexes 4 and 5.

Given the number of contracts and grants from the DoD and HHS to Sarepta, it is highly likely that many of the 91 patents assigned to Sarepta which do not report federal government funding have failed to disclose such funding.

Remedies for non-disclosure of the eteplirsen patents

The legal issues regarding the obligations to disclose federal funding and the remedies available to the federal government when patents are not timely disclosed are described in the KEI Briefing Note: 2018:1, which is attached to this document.

In the case of the patents to eteplirsen, the most useful action would be for the NIH to take title to the patents that have not disclosed federal funding, and to use the ownership of those patents as leverage to lower the price of Exondys 51, in order to expand access and reduce the financial hardships faced by patients.

Attachments

“Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions,” KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018.

Annex 1: Foreign government funding of research

This case illustrates an area for potential future cooperation between the United States and other governments, as regards government rights in patents.

Several foreign governments have funded research that led to the development of Exondys 51.

Academisch Ziekenhuis Leiden, in the Netherlands, is an institution that receives research funding from the Dutch government and the European Union.¹²

The University of Western Australia also reported DMD-related funding from the Western Australia Medical and Health Research Infrastructure Fund (MHRIF).

The European Commission and several other European governments continue to fund research on DMD and many other diseases and conditions. For example, the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR) supported a clinical trial ([NCT00844597](#)) for AVI-4658 (Exondys 51).¹³

Funded by the Medical Research Council and Sarepta Therapeutics, the consortium designed an early clinical study to obtain critical proof-of-concept data for an antisense oligonucleotide or a 'molecular patch' for DMD. The 'molecular patch' was used to induce exon-skipping of exon 51 in the DMD gene, which is known to lead to the production of functional dystrophin. Increasing the levels of functional dystrophin protein could improve treatment outcomes in patients with DMD who possess the appropriate genotype. . .

Dr Edward Kaye, Chief Medical Officer and Senior Vice President of Sarepta Therapeutics, said: "This partnership helped us to rapidly move forward development of Eteplirsen. The University College London also gave us access to the expertise within the NIHR clinical research infrastructure. As a state of the art research facility, the NIHR Great Ormond Street Biomedical Research Centre provided a single location to analyse samples from multiple sites. This gave us a better handle on data quality and a clearer understanding of the progression of the phase I-II study."

¹² SCOPE-DMD, Project ID: [601573](#), Funded under: FP7-HEALTH.

¹³ [Duchenne muscular dystrophy - a stratified approach](#): NIHR researchers collaborate with industry partners to develop a novel therapy to improve treatment outcomes in DMD patients who possess an appropriate genotype. NIHR.

An agreement among governments on the government financing of biomedical R&D, as has been proposed for the World Health Organization, could include provisions for cross-licensing government rights in patents.

Annex 2: Sarepta Therapeutics sale of priority review voucher for Exondys 51

In considering the adequacy of the incentives to Sarepta Therapeutics for its investments in drug development, note that Sarepta obtained an FDA priority review voucher (PRV) for Exondys 51, which it sold to Gilead in February 2017 for \$125 million.

Sarepta Therapeutics Form 10-Q, June 30, 2017

3. GAIN FROM SALE OF PRIORITY REVIEW VOUCHER In February 2017, the Company entered into an agreement with Gilead Sciences, Inc. ("Gilead") to sell the Company's Rare Pediatric Disease Priority Review Voucher ("PRV"). The Company received the PRV when EXONDYS 51 was approved by the FDA for the treatment of patients with DMD amenable to exon 51 skipping. Following the early termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, in March 2017, the Company completed its sale of the PRV to a subsidiary of Gilead. Pursuant to the Agreement, the subsidiary of Gilead paid the Company \$125.0 million, which was recorded as a gain from sale of the PRV as it did not have a carrying value at the time of the sale.

Annex 3: Excerpts from the license agreement between the University of Western Australia and Sarepta Therapeutics

EX-10.1 2 d511409dex101.htm EX-10.1

Exhibit 10.1

EXECUTION VERSION

AMENDED AND RESTATED EXCLUSIVE LICENSE AGREEMENT

THIS AMENDED AND RESTATED EXCLUSIVE LICENSE AGREEMENT ("Agreement") is effective as of November 24, 2008 (the "Effective Date"), and is restated as of this 10th day of April, 2013 ("Restatement Date") by and between **THE UNIVERSITY OF WESTERN AUSTRALIA**, a body corporate established pursuant to the provisions of The University of Western Australia Act 1911, with offices at 35 Stirling Highway, Crawley, Western Australia 6009 ("UWA"), on the one hand, and **SAREPTA THERAPEUTICS**, with offices at 245 First Street Suite 1800 Cambridge, MA 02142 USA ("Sarepta") and **Sarepta International CV** ("Sarepta Netherlands," and collectively with Sarepta, "Licensee"), on the other hand.

...

C. Licensee is in the process of developing various products for the treatment of muscular dystrophy arising from defects in the dystrophin gene by inducing the skipping of certain exons in such gene for which the Patent Rights and Technical Information may be useful.

D. UWA and Licensee entered into a certain Exclusive License Agreement, dated as of the Effective Date (the "Prior License Agreement"), pursuant to which UWA granted to Licensee certain exclusive license rights under certain patent rights and technical information relating to the treatment of Duchenne muscular dystrophy by inducing the skipping of certain specified exons or blocks of exons through the use of certain specified antisense sequences (the "Prior License Rights").

E. Licensee and UWA desire to expand the Prior License Rights to allow Licensee to conduct research in the Field of Use, and to develop, manufacture, use and sell Products in the Field of Use, using the Patent Rights and Technical Information (as each term is defined below) in accordance with the terms of this Agreement, and UWA desires to have the Patent Rights and the Technical Information developed, used and commercialized in the Field of Use by Licensee. Other than the rights expressly granted by UWA hereunder within the Field of Use, Licensee acknowledges that UWA shall retain all other rights with respect to the Patent Rights and the Technical Information.

. . .

(c) with respect to the Patent Rights, UWA has been assigned all right, title and interest from the Inventors and UWA is listed as the sole owner of record in the records of the United States Patent and Trademark Office and any foreign patent offices with respect to Patent Rights that consist of applications or registrations with such offices,

. . .

(f) the Patent Rights have been duly prepared, filed, prosecuted, obtained, and maintained in accordance with all applicable laws, rules, and regulations;

(g) to the best of UWA's knowledge, and except as specified on Schedule 3.1, no third party's intellectual property rights would be infringed or misappropriated by the practice of the Patent Rights in general and no third party is infringing or misappropriating the Patent Rights;

Annex 4: Patents assigned to Antivirals, Inc., AVI BioPharma or Sarepta Therapeutics which either declare government funding or share an assignment to a U.S. government agency

PAT. NO.	Government Rights	Title
<u>9.833.468</u>	Joint assignment to DHHS	Methods for treating progeroid laminopathies using oligonucleotide analogues targeting human LMNA
<u>9.394.323</u>	HDTRA1-09-C-0046 and HDTRA1-C-10-0079, DoD	Antisense antiviral compound and method for treating influenza viral infection
<u>9.326.992</u>	Joint assignment to DHHS	Methods for treating progeroid laminopathies using oligonucleotide analogues targeting human LMNA
<u>8.759.307</u>	NS 41219, AI 43103, AI 25913 from NIH, HHSN266200400058C, HHS	Oligonucleotide compound and method for treating nidovirus infections
<u>8.697.858</u>	HDTRA1-09-C-0046 and HDTRA1-C-10-0079, DoD	Antisense antiviral compound and method for treating influenza viral infection
<u>8.357.664</u>	R01 AI056267, NIH	Antisense antiviral compound and method for treating influenza viral infection
<u>8.168.604</u>	Joint assignment to Army Medical Research and Materiel Command	Antisense antiviral compounds and methods for treating a filovirus infection
<u>8.030.292</u>	Joint assignment to Army Medical Research and Materiel Command	Antisense antiviral compounds and methods for treating a filovirus infection
<u>8.030.291</u>	Joint assignment to Army Medical Research and Materiel Command	Antisense antiviral compounds and methods for treating a filovirus infection
<u>7.582.615</u>	Joint assignment to DHHS	Antisense antiviral compound and method for treating arenavirus infection

Annex 5: Patents assigned to Antivirals, Inc., AVI BioPharma or Sarepta Therapeutics with no disclosures of federal funding

PAT. NO.	Title
9,920,085	Boronic acid conjugates of oligonucleotide analogues
9,862,946	Peptide oligonucleotide conjugates
9,790,499	Functionally-modified oligonucleotides and subunits thereof
9,682,097	Oligonucleotide analogues targeting human LMNA
9,572,899	Compositions for enhancing transport of molecules into cells
9,534,220	Antisense antibacterial method and compound
9,506,058	Compositions for treating muscular dystrophy
9,499,583	Antibacterial antisense oligonucleotide and method
9,487,786	Immunosuppression compound and treatment method
9,469,664	Oligonucleotide analogues having modified intersubunit linkages and/or terminal groups
9,453,225	Multiple exon skipping compositions for DMD
9,447,417	Multiple exon skipping compositions for DMD
9,447,416	Multiple exon skipping compositions for DMD
9,434,948	Multiple exon skipping compositions for DMD
9,416,361	Splice-region antisense composition and method
9,382,536	Antisense antiviral compounds and methods for treating a filovirus infection
9,347,063	Oligonucleotide analog and method for treating flavivirus infections
9,278,987	Functionally-modified oligonucleotides and subunits thereof
9,249,243	Antibacterial antisense oligonucleotide and method
9,238,042	Antisense modulation of interleukins 17 and 23 signaling
9,234,198	Multiple exon skipping compositions for DMD
9,217,148	Exon skipping compositions for treating muscular dystrophy
9,161,948	Peptide oligonucleotide conjugates
9,157,081	Chimeric oligomeric compounds for modulation of splicing
9,068,185	Antisense modulation of nuclear hormone receptors
9,066,967	Oligonucleotide analogues targeting human LMNA
8,933,216	Immunosuppression compound and treatment method
8,906,872	Antisense antiviral compound and method for treating ssRNA viral infection
8,895,722	Splice-region antisense composition and method
8,877,725	Peptide conjugated, inosine-substituted antisense oligomer compound and method
8,871,918	Multiple exon skipping compositions for DMD
8,865,883	Multiple exon skipping compositions for DMD
8,835,402	Compound and method for treating myotonic dystrophy
8,785,410	Antisense composition and method for treating muscle atrophy

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<u>8.785.407</u>	Antisense antiviral agent and method for treating ssRNA viral infection
<u>8.779.128</u>	Oligonucleotide analogues having modified intersubunit linkages and/or terminal groups
<u>8.741.863</u>	Compound and method for treating myotonic dystrophy
<u>8.703.735</u>	Antisense antiviral compounds and methods for treating a filovirus infection
<u>8.618.270</u>	Oligonucleotide analog and method for treating flavivirus infections
<u>8.592.386</u>	Antisense compositions and methods for modulating contact hypersensitivity or contact dermatitis
<u>8.536.147</u>	Antibacterial antisense oligonucleotide and method
<u>8.524.684</u>	Antisense antiviral compounds and methods for treating a filovirus infection
<u>8.524.676</u>	Method for treating enterovirus or rhinovirus infection using antisense antiviral compounds
<u>8.501.704</u>	Immunosuppression compound and treatment method
<u>8.501.703</u>	Chimeric oligomeric compounds for modulation of splicing
<u>8.436.163</u>	Splice-region antisense composition and method
<u>8.415.313</u>	Antisense oligomers and methods for inducing immune tolerance and immunosuppression
<u>8.329.668</u>	Antisense antiviral compound and method for treating picornavirus infection
<u>8.314.072</u>	Antisense antibacterial method and compound
<u>8.299.206</u>	Method of synthesis of morpholino oligomers
<u>8.198.429</u>	Antisense antiviral compounds and methods for treating a filovirus infection
<u>8.129.352</u>	Antisense antiviral compound and method for treating ssRNA viral infection
<u>8.084.433</u>	Antisense antiviral compound and method for treating ssRNA viral infection
<u>8.076.476</u>	Synthesis of morpholino oligomers using doubly protected guanine morpholino subunits
<u>8.067.571</u>	Antibacterial antisense oligonucleotide and method
<u>8.067.569</u>	Splice-region antisense composition and method
<u>8.053.420</u>	Peptide conjugated, inosine-substituted antisense oligomer compound and method
<u>8.008.469</u>	Antisense compound for inducing immunological tolerance
<u>7.989.608</u>	Immunomodulatory agents and methods of use
<u>7.943.762</u>	Oligonucleotide analogs having cationic intersubunit linkages
<u>7.888.012</u>	Antisense composition and method for treating muscle atrophy
<u>7.884.194</u>	Soluble HER2 and HER3 splice variant proteins, splice-switching oligonucleotides, and their use in the treatment of disease
<u>7.855.283</u>	Antisense antiviral compound and method for treating arenavirus infection
<u>7.807.801</u>	Oligonucleotide analog and method for treating flavivirus infections
<u>7.790.694</u>	Antisense antibacterial method and compound
<u>7.754.238</u>	Delivery of microparticle-conjugated drugs for inhibition of stenosis
<u>7.625.873</u>	Antisense antibacterial method and compound
<u>7.524.829</u>	Antisense antiviral compounds and methods for treating a filovirus infection
<u>7.507.196</u>	Antisense antiviral compounds and methods for treating a filovirus infection
<u>7.468.418</u>	Compositions for enhancing transport of molecules into cells
<u>7.402.574</u>	Antisense composition and method for treating cancer

KEI Series on patents that fail to disclose U.S. government funding

<u>7,264,925</u>	Method for analysis of oligonucleotide analogs
<u>7,238,675</u>	Antisense antibacterial method and composition
<u>7,115,583</u>	Microbubble compositions and methods for oligonucleotide delivery
<u>7,094,765</u>	Antisense restenosis composition and method
<u>7,049,431</u>	Antisense antibacterial cell division composition and method
<u>6,869,795</u>	Antisense compositions and cancer-treatment methods
<u>6,841,542</u>	Transforming growth factor beta (TGF-.beta.) blocking agent-treated stem cell composition and method
<u>6,828,105</u>	Antisense antiviral agent and method for treating ssRNA viral infection
<u>6,784,291</u>	Splice-region antisense composition and method
<u>6,764,680</u>	Combined approach to treatment of cancer with hCG vaccines
<u>6,677,153</u>	Antisense antibacterial method and composition
<u>6,365,577</u>	p53 antisense agent and method
<u>6,365,351</u>	Non-invasive method for detecting target RNA
<u>6,124,271</u>	Method and conjugate for treating H. pylori infection
<u>6,060,246</u>	Reagent and method for isolation and detection of selected nucleic acid sequences
<u>6,030,941</u>	Polymer composition for delivering substances in living organisms
<u>5,698,685</u>	Morpholino-subunit combinatorial library and method
<u>5,521,063</u>	Polynucleotide reagent containing chiral subunits and methods of use
<u>5,506,337</u>	Morpholino-subunit combinatorial library and method
<u>5,378,841</u>	Alpha-morpholino ribonucleoside derivatives and polymers thereof

Annex 6: Selected exhibits of Sarepta Therapeutics SEC filings

Description	Form	Exhibit	Filing Date
Agreement between AVI BioPharma, Inc. and the U.S. Defense Threat Reduction Agency dated May 5, 2009.	10-Q	10.72	8/10/09
Amended and Restated Exclusive License Agreement by and among The University of Western Australia, Sarepta Therapeutics, Inc., and Sarepta International CV dated April 10, 2013.	10-Q	10.1	5/9/13
Amended and Restated Executive Employment Agreement dated April 19, 2013 by and between Sarepta Therapeutics, Inc. and Christopher Garabedian.	10-Q	10.2	5/9/13
Amendment No. 1 to the License and Collaboration Agreement between Summit (Oxford) Ltd. and Sarepta Therapeutics Inc. dated June 13, 2017	10-Q	10.1	8/3/17
Amendment No. 2 to Employment Agreement with Patrick Iversen, Ph.D., dated January 18, 2010.	10-K	10.6	3/15/11
Amendment of Contract between AVI BioPharma, Inc. and the U.S. Defense Threat Reduction Agency (contract no HDTRA 1-09-C-0046), effective March 25, 2010.	10-Q	10.81	5/10/10
Amendment of Contract between AVI BioPharma, Inc. and the U.S. Defense Threat Reduction Agency (contract no. HDTRA 1-07-C0010), effective September 30, 2009.	10-Q	10.77	11/9/09
Amendment of Contract between AVI BioPharma, Inc. and the U.S. Defense Threat Reduction Agency (contract no. HDTRA1-07-C-0010), effective May 29, 2009.	10-Q	10.74	8/10/09
Amendment to Employment Agreement with Patrick Iversen, Ph.D., dated December 28, 2008.	10-K	10.5	3/15/11
Asset Purchase Agreement dated February 20, 2017 by and between Sarepta Therapeutics Inc. and Gilead Sciences, Inc.	10-Q	10.1	5/4/17
Collaboration and License Agreement between Isis Pharmaceuticals and Ercole Biotech, Inc. dated May 16, 2003.	10-K	10.78	3/16/10
Consulting Agreement dated August 17, 2017 by and between Sarepta Therapeutics, Inc. and Dr. Edward M. Kaye	10-Q	10.1	11/1/17
Contract Number HDTRA1-10-C-0079 between Defense Threat Reduction Agency and AVI BioPharma, Inc. dated June 4, 2010.	10-Q	10.84	8/9/10
Contract Number W9113M-10-C-0056 between U.S. Army Space and Missile Defense Command and AVI BioPharma, Inc. dated July 14, 2010.	10-Q	10.86	11/9/10
Contract Number W911QY-12-C-0117 between U.S. Department of Defense's Joint Project Manager Transformational Medical Technologies and Sarepta Therapeutics, Inc. dated August 23, 2012.	10-Q	10.1	11/7/12
Employment Agreement dated September 20, 2016 between Sarepta Therapeutics, Inc. and Edward M. Kaye, M.D.	10-Q	10.1	11/7/16
Employment Agreement with Patrick Iversen, Ph.D., dated July 14, 1997.	10KSB	10.12	3/30/98

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Exclusive License Agreement by and between The University of Western Australia and AVI BioPharma, Inc., dated November 24, 2008.	10-K	10.36	3/15/11
Executive Employment Agreement dated June 13, 2011 by and between AVI BioPharma, Inc. and Edward Kaye, M.D.	10-Q	10.4	8/8/11
First Amendment to License Agreement by and among The University of Western Australia, Sarepta Therapeutics, Inc., and Sarepta International CV dated June 19, 2016.	10-Q	10.1	8/9/16
First Amendment to Sponsored Research Agreement between AVI BioPharma, Inc. and Charley's Fund, Inc. dated June 2, 2009.	10-Q	10.75	8/10/09
License Agreement between Sarepta Therapeutics, Inc. and Sarepta International C.V. on the one hand and BioMarin Leiden Holding BV, BioMarin Nederlands BV and BioMarin Technologies BV on the other hand dated July 17, 2017	10-Q	10.8	8/3/17
License and Collaboration Agreement between Summit (Oxford) Ltd and Sarepta Therapeutics, Inc. dated October 3, 2016	10-Q	10.2	11/7/16
Modification No. P00005 to Contract Number HDTRA1-10-C-0079 between Defense Threat Reduction Agency and AVI BioPharma, Inc. effective April 13, 2011.	10-Q	10.1	8/8/11
Modification No. P00005 to Contract Number W9113M-10-C-0056 between U.S. Army Space and Missile Defense Command and AVI BioPharma, Inc. effective August 15, 2011.	10-Q/A	10.3	2/15/12
Modification No. PZ0001 to Contract Number HDTRA1-10-C-0079 between Defense Threat Reduction Agency and AVI BioPharma, Inc. effective March 3, 2011.	10-Q	10.3	5/10/11
Settlement Agreement between Sarepta Therapeutics, Inc., Sarepta International C.V. and The University of Western Australia on the one hand, and BioMarin Leiden Holding BV, BioMarin Nederlands BV and BioMarin Technologies BV on the other hand dated July 17, 2017	10-Q	10.7	8/3/17
Sponsored Research Agreement between AVI BioPharma, Inc. and Charley's Fund, Inc., effective October 12, 2007.	10-K	10.58	3/17/08

DRAFT

Mr. James Love
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, D.C. 20009

Sent By Email: james.love@keionline.org

Subject: KEI April 5, 2018 Letter to HHS Secretary Azar on Exondys 51

Dear Mr. Love:

The National Institutes of Health (NIH) is responding to your April 5, 2018 request that was signed by Knowledge Ecology International (KEI) and five other organizations (KEI Request) to Secretary Azar concerning Exondys 51®. The KEI Request asked that Health and Human Services (HHS) exercise its rights under the Bayh-Dole Act to take title to five patents on eteplirsen, as a remedy to a failure by the University of Western Australia to disclose NIH funding of the inventions, and to use the ownership of those patents as leverage to obtain lower prices to Exondys 51®.

NIH is currently reviewing the information KEI provided along with, NIH funding records, disclosures to NIH of any applicable inventions, the U.S. Patent and Trademark Office records, and any other relevant documents. When NIH's analysis is completed we will notify you.

Sincerely,

cc: Health GAP
Patients for Affordable Drugs
People of Faith for Access to Medicines
Social Security Works
Universities Allied for Essential Medicines
HHS OIG - Daniel R. Levinson

REL0000023655.0004

From: Ferriter, Karin [Karin.Ferriter@USPTO.GOV]
Sent: 6/6/2018 10:20:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Legal/regulatory restrictions on transfers of NIH-funded IP

FYI

From: James Love <james.love@keionline.org>
Sent: Wednesday, June 6, 2018 2:40 PM
To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>; Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Cc: Andrew Goldman <andrew.goldman@keionline.org>; robert.silverman@oxfam.org; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Karen Rogers,

In case it was not explained before, we are interested in knowing if the NIH has a policy that would prevent a company from transferring an NIH funded license to an entity in order to avoid paying U.S. income taxes.

Are you saying that the NIH has no interest in regulating transactions that allow patent holders of NIH funded inventions to evade U.S. income taxes on inventions, or are you saying that you don't want to talk to us? Or both?

Jamie

On Wed, Jun 6, 2018 at 8:24 PM, Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov> wrote:

Dear Mr. Goldman – Thank you for your inquiry.

We don't have any interest in such a discussion and I'm afraid that we don't have any suggestions for a different office at NIH that would. Regards, Karen

Karen L. Rogers

Acting Director

Office of Technology Transfer

National Institutes of Health

6011 Executive Boulevard, Suite 325

REL0000024154

Rockville, MD 20852

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]
Sent: Monday, May 07, 2018 4:11 PM
To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: robert.silverman@oxfam.org; Jamie Love <james.love@keionline.org>
Subject: Legal/regulatory restrictions on transfers of NIH-funded IP

Dear Karen, Ann:

I have cc'd Robert Silverman of Oxfam, and James Love of KEI, as we had hoped to have a conversation with you regarding the NIH's authority to restrict offshore transfers of NIH-funded intellectual property from a company to a subsidiary or affiliate.

Would you have time for a phone call on this? If there is a different office in NIH that you think would be more appropriate for this conversation, please let us know.

Kind regards,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: [+1.202.332.2670](tel:+12023322670)

www.keionline.org

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REL0000024154

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Plude, Denise (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=91F83D681D984EAA8FE3DE287AEBFA01-PLUDEDE]
Sent: 12/29/2017 6:02:34 PM
To: Jorgenson, Lyric (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3bbde7d361374981a4d336b6eeb17521-jorgensonla]; Fennington, Kelly (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c3e2d306aa244429b0f51d365bd24a26-fenningk]; Paltoo, Dina (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afbb60a3cbcd495aa92790a75dc3ffd6-paltoo]; Tucker, Jessica (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2baf4ae78d90412dbefbfb5e52c31a4-tuckerjm]; Volkov, Marina (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d1b73452d01f4998b0f065c4c0b62449-mvolkov]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Bayha, Ryan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5d5a4353cd514322a8598dbb1751ee79-bayhar]
CC: Wertz, Jennifer (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1e6cb9797cef40f1b40e777afe3795d7-wertzj]; Ampey, Bryan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9672b522d0b34f3792e2934dac636a57-ampeybc]
Subject: DDRMS FYIs
Attachments: 368387D.pdf; 368387E.pdf; 369387.pdf; 369387A.pdf; 369387B.pdf; 369387C.pdf; 369413.pdf; 369413A.pdf; 369249.pdf; 369249A.pdf; 369249B.pdf; 369249C.pdf; 369249D.pdf; 369249E.pdf; 369249F.pdf; 369249G.pdf; 369249H.pdf; 369249I.pdf; 369249J.pdf; 369249K.pdf; 369249L.pdf; 369249 final email.pdf; 369249 tables.pdf; Letter regarding DHHS policy on licensing of CRISPR patents

Work Folder Information this one is the attachment name "Letter regarding DHHS policy on licensing of CRISPR patents

Work Folder: WF 365590

Process: FYI

Program Analyst: Boskent, Celeste (NIH/OD) [E]

Due Date:

WF Subject: Letter regarding DHHS policy on licensing of CRISPR patents.

IC: od_osp

From: Love, James

To: Collins, FrancisPrice, Tom

Remarks: FYI: OSP and NHGRI. May return for OS response creation.

Work Folder Information

Work Folder: WF 369387

Process: FYI

Program Analyst: Whitfield, Michelle D. (NIH/OD) [E]

Due Date:

WF Subject: OS FYI- Recommendations from Secretary's Advisory Committee on Human Research Protections SACHRP.

IC: od_osp

From: Wright, Donald

To: Hargan, Eric D.Agnew, Ann C.Stannard, Paula M.

Remarks: FYI for OER, OSP, ORWH, NICHD, and OIR.

Work Folder Information**Work Folder:** WF 369413**Process:** FYI**Program Analyst:** Hurlebaus, Lisa (NIH/OD) [E]**Due Date:****WF Subject:** Letter from 62 organizations to President Trump re: America Falls Behind in Hepatitis Elimination Efforts.**IC:** od_osp**From:** Huriaux, Emalie**To:** Trump, Donald J.**Remarks:** FYI to FIC, NIAID (Dr. Fauci was cc'd), NIDA, NIDDK (Dr. Rodgers was cc'd), OLPA, and OSP.**Work Folder Information****Work Folder:** WF 369249**Process:** FYI**Program Analyst:** Mason, Karen (NIH/OD) [E]**Due Date:****WF Subject:** Sandra Schmid (UT Southwestern Medical Center) email regarding perceived continuing gender bias at NIH. Voices concerns that October announcement of NIH Directors Pioneer Award new recipients appear to include 11 men and 1 woman.**IC:** od_osp**From:** Schmid, Sandra**To:** Collins, Francis**Remarks:** Assigned to DPCPSI, COSWD, EDI, CSR, OER, OIR, OCPL, OGC, ORWH, and OSP. Please note Dr. Collins' email response located in the Final Response Folder

From: jamespackardlove@gmail.com [jamespackardlove@gmail.com]
on behalf of Jamie Love [james.love@keionline.org]
Sent: 6/5/2017 6:22:51 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Price, Thomas (HHS/OS) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=be726e39e5004b5ea07f712386ffed24-Thomas.Pric]
CC: Andrew S. Goldman [andrew.goldman@keionline.org]; Diane Singhroy [diane.singhroy@keionline.org]; Claire Cassedy [claire.cassedy@keionline.org]; Manon Ress [manon.ress@keionline.org]; Thiru Balasubramaniam [thiru@keionline.org]
Subject: Letter regarding DHHS policy on licensing of CRISPR patents
Attachments: CRISPR-SecPrice-6Jan2017.pdf

Dear Secretary Price and NIH Director Francis Collins,

Attached is a letter from KEI asking DHHS to develop a policy on the licensing of CRISPR patents.

James Love
Director
Knowledge Ecology International

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 12/19/2017 8:36:54 PM
To: Gadhia, Ami (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd345316c77427da92947ab04d5511c-gadhiaad]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Solowiej, Anna (NIH/NHGRI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=12d161a0bbdd4090b24e61708aa61afa-solowieja]; Vathyam, Surekha (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ed61806c5bf4e9a819ddb37e91dee70-vathyams]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
Subject: RE: December TDC-Short call: attachment re "Clearance for Service of a NIH Associate Research Physician or Senior Research Physician as NIH Principal Investigator for CRADA"
Attachments: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Ami and Mark,

The workshop concept I described back in November (attached) was covered very well by Mark during his NCI webinar last week. [REDACTED] b5

[REDACTED] b5

Mark has been assisting us with our recent efforts to [REDACTED] b5 Our efforts are in progress, but I plan to provide a window into our experience [REDACTED] b5

Does this seem sensible?

Mike

From: Gadhia, Ami (NIH/NCATS) [E]
Sent: Friday, December 15, 2017 10:26 AM
To: NIH TDC Short <niaaatdcs-l@mail.nih.gov>
Cc: Gerfen, Charles (NIH/NIMH) [E] <gerfenc@mail.nih.gov>; Vathyam, Surekha (NIH/NCI) [E] <vathyams@mail.nih.gov>
Subject: December TDC-Short call: attachment re "Clearance for Service of a NIH Associate Research Physician or Senior Research Physician as NIH Principal Investigator for CRADA"

All:

We'll be having our regularly scheduled TDC-Short call next Wednesday, December 20th from 11:30 am – 1 pm. The agenda is copied and pasted below, and is included in the meeting invite that I sent as well.

December TDC Short Meeting Agenda:

1. Charles Gerfen, NIMH: Clearance for Service of a NIH Associate Research Physician or Senior Research Physician as NIH Principal Investigator for CRADA
2. Jenny Wong: updating RDFs to reflect current patent status
3. Mike Mowatt: possible workshop idea
4. AOB

First off, Chip Gerfen will speak to us about the topic listed above. Please review the attached document related to that agenda item, in advance of our call, if you are available to do so.

Also, as you know, I'll be rolling off as Vice Chair at the end of 2017. We will welcome Surekha Vathyam as your new TDC Vice Chair for 2018. Surekha is a pleasure to work with, and I'm sure you all will enjoy her moderating the TDC-Short calls going forward.

Best regards,

Ami Gadhia, J.D., LL.M., C.L.P.

Technology Transfer and Patenting Specialist

(301) 827-7159 * Note new number

Ami.gadhia@nih.gov

Office of Strategic Alliances

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National Institutes of Health (NIH)

NIH NCATS: Improving Health Through Smarter Science

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From: Gadhia, Ami (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD345316C77427DA92947AB04D5511C-GADHIAAD]
Sent: 11/13/2017 2:05:56 PM
To: Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Hi Mike,

Hope you had a nice long weekend.

Could I please add your topic below to the December agenda, since this month's agenda is heavy with a presentation and time-sensitive discussions? Thanks for your consideration.

Best,
Ami

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Friday, October 6, 2017 1:59 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Gadhia, Ami (NIH/NCATS) [E] <ami.gadhia@nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Understood. I meant others at NIH, not outside NIH.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, October 6, 2017 1:20 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Gadhia, Ami (NIH/NCATS) [E] <ami.gadhia@nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Also note that, if we include outside people, we cannot discuss internal deliberations and discussions of what we would or would not do with them present.

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Friday, October 06, 2017 12:53 PM
To: Gadhia, Ami (NIH/NCATS) [E] <ami.gadhia@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>
Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Happy to make the suggestion. When's the next meeting? I'm not available on 11 Oct.

Enjoy a nice long weekend!!

From: Gadhia, Ami (NIH/NCATS) [E]
Sent: Friday, October 6, 2017 12:49 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E]

<rohrbaum@od.nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>

Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>

Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Hi Mike,

Thanks for sharing. I personally agree that this type of workshop would be topical and interesting. Would you be willing to raise this topic at our next TDC-Short meeting, so that we may take a straw poll (and solicit potential volunteers)?

Best,
Ami

From: Mowatt, Michael (NIH/NIAID) [E]

Sent: Friday, October 6, 2017 12:01 PM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Solowiej, Anna (NIH/NHGRI) [E] <anna.solowiej@nih.gov>; Gadhia, Ami (NIH/NCATS) [E] <ami.gadhia@nih.gov>

Cc: Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>

Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

Thanks for sharing this, Mark.

Anna and Ami,

I wonder whether an organized discussion of these efforts and activities over the past year or so would be beneficial for our community.

Some possible objectives for such a discussion:

b5

Joe Allen's talk next week will provide great background for this discussion.

We may want to consider:

b5

b5

Mike

From: Rohrbaugh, Mark (NIH/OD) [E]

Sent: Friday, October 6, 2017 10:17 AM

To: NIH TDC Short <niaaatdcs-l@mail.nih.gov>

Subject: FW: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

b5

"In exceptional circumstances, and in the event that the Licensed Patent Rights are Subject Inventions made under a CRADA, the Government, pursuant to 15 U.S.C. §3710a(b)(1)(B), retains the right to require the Licensee to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the Licensed Patent Rights in the Licensed Field of Use on terms that are reasonable under the circumstances, or if the Licensee fails to grant this license, the Government retains the right to grant the license itself. The exercise of these rights by the Government shall only be in exceptional circumstances and only if the Government determines:

- (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by the Licensee;
- (ii) the action is necessary to meet requirements for public use specified by Federal regulations, and these requirements are not reasonably satisfied by the Licensee; or
- (iii) the Licensee has failed to comply with an agreement containing provisions described in 15 U.S.C. §3710a(c)(4)(B);

-Mark

<http://www.keionline.org/node/2867>

KEI asks HHS to use Bayh-Dole rights in Zinbryta patent (drug for multiple sclerosis)

Submitted by KEI Staff on 14. September 2017 - 12:30

- [Medical Technologies](#)

Attached is a letter sent on September 14, 2017 to Andrew Bremberg, an Assistant to the President and the Director of the Domestic Policy Council at the White House, and Keagan Lenihan, a Senior Adviser to HHS Secretary Tom Price, regarding Zinbrytra (INN: daclizumab), a drug to approved by the FDA to treat multiple sclerosis. (PDF version [here](#))

This is an older drug, and the NIH obtained a patent on its use to treat multiple sclerosis, and licensed the patent on a exclusive basis to Biogen. Biogen and Abbvie market the drug around the world. The price in the United States is more than \$96,000 per year (\$7390 per injection every 4 weeks, 13 times a year), but far lower in every high income country where KEI obtained prices.

The letter asks DHHS to use one or more of three federal rights in the NIH licensed patent to "authorize affordable competition, or to force Biogen to lower its price." The three actions include using the royalty free right in the patent, exercising march-in rights, or terminating the license. The option to terminate the license is featured in the letter, and it is an action that KEI had not focused on previously.

The termination clause is something the U.S. government can do with government owned patents, including any owned by the NIH.

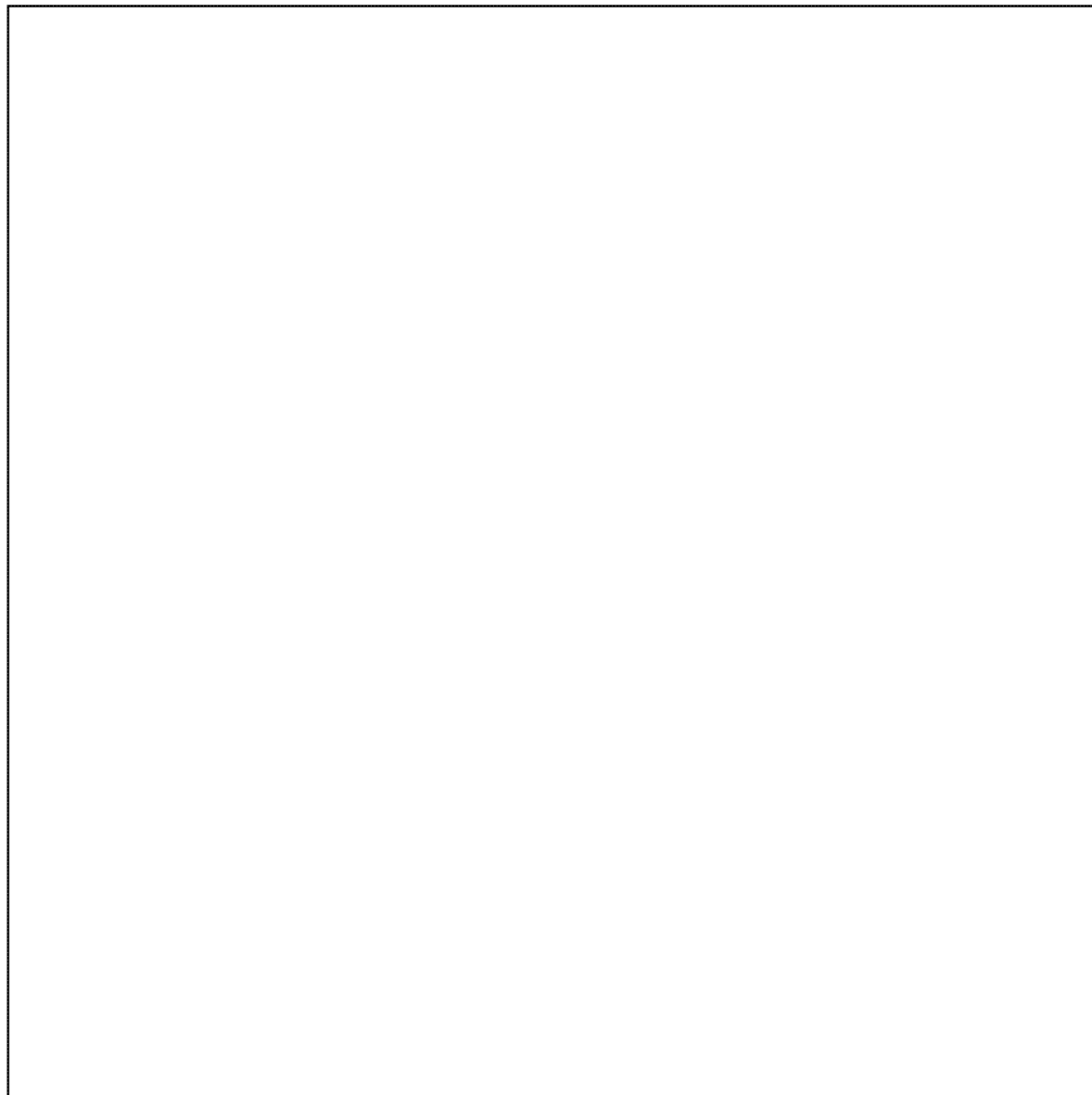
At the end of this blog is a graph of the prices of MS drugs, over time.

Below is an excerpt from the beginning and another excerpt from the end of the letter.

We write to you today with regard to the excessive price of an important drug for multiple sclerosis called daclizumab, co-marketed by Biogen and AbbVie as Zinbryta at prices roughly 3 to 4 times higher in the United States than in other high income countries. The patent for Zinbryta was licensed from the NIH, and under the Bayh-Dole Act there are three specific actions the United States government can and should utilize to authorize affordable competition, or to force Biogen to lower its price. These include: (1) making use of the government's royalty-free rights in the patent; (2) utilizing the "march-in" right to license the patent to a third party; and/or (3) terminating the exclusive license.

Amidst a crisis of out-of-control drug prices, this is an instance where the federal government has the power to act without the need for any additional statutory authority.

[snip]



[snip]

The United States prices are 2.8 to 4.3 times higher than any of the reference countries. The U.S. price is 2.8 times higher than Norway and Denmark and 3.8 times higher than Switzerland, even though all three of these countries have higher per capita incomes than the United States, and the U.S. taxpayers funded the relevant discovery and own the patent.

There is no reason to accept a foreign price, even from a country of a similar per capita income, as reasonable. But in our opinion, it is unreasonable for Biogen/Abbvie to charge higher prices in the United States than in other large economies with a per capita income at least 50 percent of the United States.

In this case, prices in the U.S. are not only higher — they are 180 to 330 percent higher than every high income country where KEI could obtain pricing data. The pricing of Zinbryta is contrary to statutory requirement of the Bayh-Dole Act to make the inventions available to the public on reasonable terms.

A failure by HHS to address the discrimination against U.S. residents in pricing harms everyone who buys or reimburses the drugs, including all U.S. taxpayers, all employers who pay for health benefits, and many persons living with multiple sclerosis who face daunting co-payments, who are underinsured, or who never get the drug because of its high cost.

Conclusion

We request that the Department of Health and Human Services use one or more of the three options at its disposal under the Bayh Dole Act to lower prices of this important MS drug, including:

- (1) under 35 U.S.C. § 209(d)(1), utilizing the royalty-free license in the government-owned patent to authorize generic competition;
- (2) under 35 U.S.C. § 203(a), utilizing the “march-in” rights to license the drug to a third party; or
- (3) 35 U.S.C. § 209(d)(3), terminating the exclusive NIH license to Abbott/Biogen on the ground that the company is failing to abide by its obligation to make to invention “available to the public on reasonable terms”.

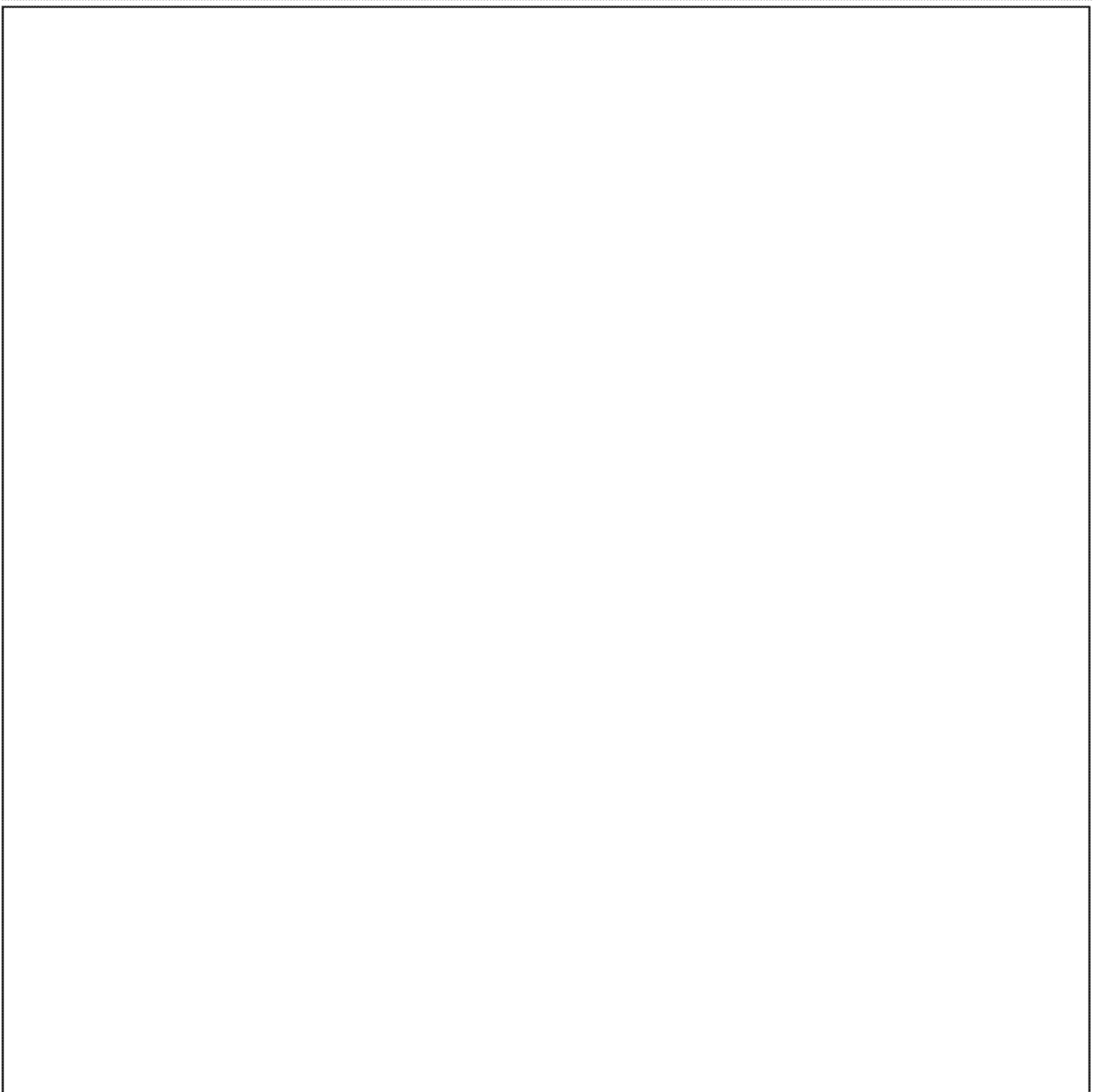
Specifically, this letter should be seen as request to exercise march-in rights under 35 U.S.C. § 203(a), and/or to terminate the license under 35 U.S.C. § 209(d)(3), on the grounds that charging U.S. residents 2.8 to 4.3 times more than residents in other high income countries is on its face unreasonable, and in violation of the requirement in 35 U.S.C. § 201(f) to make the invention covered by the license “available to the public on reasonable terms.” We also urge DHHS to use the royalty-free right in the patents to exercise leverage and freedom to operate whenever it faces challenges in implementing its section 203 or 209 rights.

We believe that terminating the exclusive license may be the best option, because it will provide the most leverage and the most flexibility in terms of obtaining alternative supplies of the product. But a credible threat to use any of these three options will be sufficient to force Biogen

and AbbVie to lower its price of Zinbryta, at least to the prices that the companies already charge in other countries with incomes similar to the United States.

The Trump Administration has made numerous public pronouncements regarding the need to fight high drug prices, a policy point supported by overwhelming public opinion. In this instance, the government has all of the leverage it needs to take strong, decisive action to benefit multiple sclerosis patients, consumers, and taxpayers.

We request a meeting at your earliest convenience to discuss this matter further.



From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 9/11/2017 2:17:11 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertson]; Whitney, Laurie (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=903a0f2d510b4ef3a081c10eef17deb8-whitney]
Subject: FW: Responses to Objecting Comments for A-381-2017
Attachments: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers to Salubris Biotherapeutics; Exclusive Patent License to Salubris Biotherapeutics, Inc.; Prospective Grant of Exclusive Patent License; Re: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers; Prospective Grant of Exclusive Patent License: Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers; Comment on "Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers"; Proposed Exclusive Patent License to Salubris Biotherapeutics

Hi Mark,

I'm following up on this question from Dave Lambertson. As you know, we've had multiple contacts about this issue, and we want to make sure that OD's perspective(s) is captured in our response. I'm copying Dave and Laurie Whitney.

Dave would like to present these findings at this Wednesday's ELCG meeting so if you can get him a quick response, it would be much appreciated.

Thanks,

Richard

From: Lambertson, David (NIH/NCI) [E]
Sent: Tuesday, September 05, 2017 6:54 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Whitney, Laurie (NIH/NCI) [E] <whitneyl@mail.nih.gov>
Subject: FW: Responses to Objecting Comments for A-381-2017

Good morning Mark,

I am following up on my e-mail from a couple of weeks ago. Please let us know how OD would like us to respond to the objecting comments. We would like to respond in the near future, as I hope to present a Final Determination on this matter at the next ELCG Meeting (13 September 2017).

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager

REL0000024245

Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

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Fax: 240-276-5504

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From: Lambertson, David (NIH/NCI) [E]
Sent: Wednesday, August 23, 2017 7:57 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: Responses to Objecting Comments for A-381-2017

Good morning Mark,

The fifteen (15) day period for objections to the Notice of Intent to Grant for license application A-381-2017 ended last night. There were eight (8) total objections, seven (7) of which were in the form of comments (the eighth was a competing application which will be analyzed and addressed separately in a Final Determination). I have attached the objecting comments that I received to this e-mail for your review. Here is a list of the commenters in order of the date of their submission, for ease of reference:

- 1) Knowledge Ecology International (KEI)
- 2) Samer Nuwayhid
- 3) David Kolstedt
- 4) Bruce Korb
- 5) Arnold Shugarman
- 6) Brinsley Davis
- 7) Paul Stumpf

Richard wanted me to contact you about providing formal responses to the objecting comments concerning our advertisement of intent to grant, particularly in view of the recent article concerning the intent to grant. My initial thought is [REDACTED]

b5

b5

[REDACTED] b5 and send each to your attention for review and comment prior to sending them.

Thanks,
Dave

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager

REL0000024245

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david.lambertson@nih.gov
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Fax: 240-276-5504

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From: jamespackardlove@gmail.com [jamespackardlove@gmail.com]
on behalf of Jamie Love [james.love@keionline.org]
Sent: 8/8/2017 11:55:55 AM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertson]; Diane Singhroy [diane.singhroy@keionline.org]; Manon Ress [manon.ress@keionline.org]
Subject: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers to Salubris Biotherapeutics
Attachments: Salubris-8August2017.pdf

Dear Dr. Lambertson,

Attached are the comments of KEI on the license to Salubris Biotherapeutics.

Could we do a call about this license. Diane thinks this technology is quite important, and the patent portfolio appears to be extensive.

Jamie

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,

twitter.com/jamie_love

From: Samer Nuwayhid [b6]
Sent: 8/8/2017 8:04:24 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: Exclusive Patent License to Salubris Biotherapeutics, Inc.

Hi Dr. Lambertson,

As a former NCI employee and current employee in biotech, I am writing to express my concerns and dislike, in regards to awarding an exclusive patent to Salubris. I disagree awarding exclusive patent license from tax-payer research to a foreign company, with no controls over pricing of the drug. Were companies in the United States, given the opportunity to compete for this exclusive patent license? In addition, why is the NIH doing this in total secrecy without feedback from the general public.

I think it is time to hold public hearings on NIH licensing practices, so we as tax-payers are not left in the dark. Thank you for your time.

Regards,
Samer Nuwayhid

From: David Kolstedt [b6]
Sent: 8/9/2017 3:35:32 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: Prospective Grant of Exclusive Patent License

I read the Huffington Post article that this license does not specify pricing obligations whatsoever. If US taxpayer dollars were used to develop the solution, then US taxpayers should benefit.

The license should contain a maximum price formula for US citizens before it is granted. I do not know enough details to specify what that formula should be but there should be a maximum price charged.

Please add this to the comments section of the NIH comments. I could not do this on-line.

Thanks for your attention,
David Kolstedt
Buffalo, MO

[b6]

From: Bruce Korb [b6]
Sent: 8/10/2017 2:53:37 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: Re: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers

Good morning Mr. Lambertson,

I am a cranky citizen who does not like to pay for research only to have the benefits of that research handed over to a private company for its exclusive benefit. What I am trying to understand is the rationale for doing so. Is the government making sure that in handing off that intellectual property that it is getting the best return for the research investment? What value is the private company giving the government for that research? Is it in the best interests of the citizenry to have a company hold exclusive patent rights and charge whatever it can get for the medicine?

So, indeed, I am not interested in the pharmacology of the drug. I likely would not understand. I am interested in the process used to get to where we are. Especially the part that made it difficult for people to comment on the proposal.

Thank you.
Regards, Bruce

On Thu, Aug 10, 2017 at 4:38 AM, Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov> wrote:

> Good morning Mr. Korb,
>
> Thank you for your e-mail. So that I may answer your e-mail appropriately, I must ask for a clarification. Is this a request for a copy of the patent/patent application, and is that the information about which you are asking why it is not available online?
>
> When I have your answers, I will prepare a response.
>
> Thank you,
>
> David A. Lambertson, Ph.D.
> Senior Technology Transfer Manager
> Technology Transfer Center
> National Cancer Institute/NIH
> david.lambertson@nih.gov
> <http://ttc.nci.nih.gov/>
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> 9609 Medical Center Drive, Rm 1-E530 MSC 9702
> Bethesda, MD 20892-9702 (USPS)
> Rockville, MD 20850-9702 (Overnight/express mail)
> Phone (Main Office): 240-276-5530
> Phone (direct): (240) 276-6467
> Fax: 240-276-5504
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> -----Original Message-----

> From: Bruce Korb [mailto:b6]
> Sent: Wednesday, August 09, 2017 4:38 PM
> To: Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
> Subject: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers

>
> Requests for copies of the patent applications, inquiries, and comments relating to the contemplated Exclusive Patent License should be directed to: David A. Lambertson, Ph.D., Senior Licensing and Patenting Manager, NCI Technology Transfer Center, 9609 Medical Center Drive, RM 1E530 MSC 9702, Bethesda, MD 20892-9702 (for business mail), Rockville, MD 20850-9702; Telephone: (240) 276-6467; Email: <david.lambertson@nih.gov>

>
> Also, please explain why the information is not online and responses are not submissable online. Thank you.

REL0000024245.0004

>
> - Bruce Korb
>
> **b6**
>

--
- Bruce

From: Arnold Shugarman [b6]
Sent: 8/10/2017 1:01:23 AM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
CC: senator@feinstein.senate.gov
Subject: Prospective Grant of Exclusive Patent License: Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers

I oppose giving an exclusive patent license to Salubris Biotherapeutics, Inc. for this drug.

If this drug was developed by NIH with taxpayers' funds, no company should be given a license to profit exclusively on this or any drug. Any agreement made by NIH or any other federal agency on drugs developed with public funding should include a profit sharing agreement with the Federal government (taxpayers).

Further, the agreement should be structured so that the price of any drug that results from granting the patent should be fair and reasonable. At the very least, the price should be set so that the drug company cannot charge American consumers more than the lowest price negotiated world-wide for the drug.

In sum, funds from American taxpayers should not be used to enrich private enterprises. It's time that Americans get a fair return on their investment of tax dollars.

Arnold Shugarman

[b6]

From: [b6]
Sent: 8/10/2017 2:20:04 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: Comment on "Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers"

Hello, Dr. Lambertson,
I have just read about this licensing proposal and I find it reckless to grant exclusive rights without ensuring that Americans will be able to buy the resulting product at a fair price. That is a bad deal for America!
You know healthcare costs are skyrocketing. You know prescription drug costs in this country are out of control. Why would the NIH do something that exacerbates these situations?
Please reconsider this deal.
Sincerely,
Brinsley Davis
Concerned Minnesota resident, zip code: [b6]

From: Paul Stumpf [b6]
Sent: 8/17/2017 7:20:56 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
Subject: Proposed Exclusive Patent License to Salubris Biotherapeutics

Dear Dr. Lambertson - I am concerned by what I have read about the proposed Exclusive Patent License proposed to be granted to Salubris - with both the terms of the license and the fact that Salubris is ultimately controlled by a wealthy Chinese. I have these concerns despite the fact that Salubris is in Gaithersburg, so that as a Maryland resident I might arguably benefit from its getting this license.

As with the proposed Zika license, I don't get giving away the benefits of taxpayer-funded research to anyone, and especially to foreign-controlled entities.

Paul Stumpf
[b6]

From: Lambert, Richard (NIH/NIAID) [C] [/O=NIH/OU=NIH/EXCHANGE/CN=NIH/NIAID/CN=LAMBERTR]
Sent: 1/27/2017 4:52:06 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: [Ip-health] Devex: Zika vaccine could be delayed, unaffordable after US Army grants exclusive rights to pharma company

Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
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-----Original Message-----

From: Zack Struver [mailto:zack.struver@keionline.org]
Sent: Friday, January 27, 2017 11:47 AM
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] Devex: Zika vaccine could be delayed, unaffordable after US Army grants exclusive rights to pharma company

<https://www.devex.com/news/zika-vaccine-could-be-delayed-unaffordable-after-us-army-grants-exclusive-rights-to-pharma-company-89519#>

Zika vaccine could be delayed, unaffordable after US Army grants exclusive rights to pharma company

By Sophie Edwards | 27 January 2017

The U.S. Army's plan to grant exclusive rights to a promising Zika vaccine to a major pharmaceutical company has raised questions about whether that threatens its future affordability and availability to people in developing countries.

The purified, inactivated Zika virus vaccine – called ZP IV – has been developed by the U.S. Army and is currently in its first phase of testing at the Walter Reed Army Institute of Research in Maryland and the National Institutes of Health.

If it successfully passes clinical trials, the vaccine would have the potential to halt the spread of the virus, transmitted by mosquitoes and sexual intercourse, which has been reported in 69 countries since 2015, including the United States, and is linked to serious birth defects in children.

The deal was posted by the Army on the public Federal Register in December and will give Sanofi Pasteur, the vaccine unit of French multinational pharmaceutical company Sanofi, exclusive access to the new vaccine technology, which has been developed and paid for by the U.S. government. In return, Sanofi will take on the role of conducting clinical trials, getting regulatory approval, manufacturing and distributing the vaccine.

The humanitarian aid organization Médecins Sans Frontières has criticized the Army's decision to grant Sanofi the patent license, which will give the company an exclusive right to make, use and sell the vaccine for 20 years, as well as 12 years of marketing and data exclusivity even after the patent has expired. MSF is saying this will give the company a monopoly on the drug and thus no incentive to make it affordable. Sanofi could also choose to stop developing the vaccine if it decides it is commercially unattractive.

MSF wants the U.S. Army to consider granting an "open nonexclusive" patent license instead, opening up the technology to other pharmaceutical companies for testing and development. MSF argues this will increase competition and thus bring down the price and ensure the vaccine reaches those who need it in middle-income and developing countries.

"Ministries of Health and people around the world will only be able to benefit from the U.S. government investment if the resulting vaccine is effective, safe, available, affordable and suitably adapted to the resource-limited settings where most people affected by Zika virus live," MSF said in a statement.

"The next step in the Zika vaccine development process, including its licensing and technology transfer strategy, needs to ensure that U.S. government funding and leadership in vaccine R&D results in a vaccine that is effective and accessible for all patients in need in the U.S. and globally, including the most neglected," the group added.

The United Nations High Level Panel on Access to Medicines, formed in 2015 to address the lack of access to medicines in many developing countries, appears to agree with MSF's recommendations. In its 2016 report, the panel said: "Universities and research institutions that receive public funding must prioritize public health objectives over financial returns in their patenting and licensing practices," and listed the use of nonexclusive licenses, the donation of IP rights, and taking part in public sector patent pools as potential mechanisms by which to do this.

Sanofi has responded by saying it's assuming "financial and opportunity risks" by partnering with the government on Zika as there is no guarantee of a commercial market for the vaccine.

"...we're still assuming financial and opportunity risks because there is no clear path to commercialization at this time, as the epidemiology of this infectious disease is still a moving target," according to Sanofi's research and development project lead, Jon Heinrichs.

The U.S. Army told Devex in an email statement: "We believe granting an exclusive license in this case is reasonable and necessary to most quickly and most safely provide this potential vaccine for public use to combat the growing international threat of the Zika virus."

Unusually, the U.S. Army has requested to extend the time period for comments on the announcement in the Federal Register by an additional 45 days until mid-March, the second time the comment period has been extended, to allow time to compose written responses to the submissions.

Experts have predicted the Zika market could be worth more than \$1 billion a year, driven by U.S. and European travelers willing to pay high prices for such vaccines, Reuters reported in October.

Sanofi is part of a race to develop a Zika vaccine

The ZP IV vaccine – which is thought to be the furthest along in terms of development in the Zika vaccine field – is developed from the inactivated Zika virus. The vaccine was shown to give 100 percent protection against the Zika virus in mice, according to a study published in science journal Nature last August.

Sanofi is not alone in working on the Zika virus vaccine. It is not even the only drug company to receive U.S. government funding to work on the issue; GlaxoSmithKline has partnered with the NIH to evaluate a new vaccine technology for Zika known as SAM (self-amplifying mRNA), and Japanese company Takeda has also entered the vaccine hunt with \$312 million funding from BARDA.

Another group of concerned organizations – including Knowledge Ecology International, a nonprofit that lobbies to increase access to medicines – have also written to the Army to complain about the Sanofi deal.

KEI says Sanofi does not need to be incentivized to develop the vaccine and take it to the market – the standard justification for granting such exclusive licenses – since the candidate vaccine has already received "extensive government subsidies" and is extremely likely to get additional funds.

"The grant of the exclusive rights in the patent is an unnecessary incentive to bring the invention to practical application because of the significant federal funding in the clinical trials and the grant of additional exclusivities and subsidies," KEI said.

In September, BARDA – the U.S. Biomedical Advanced Research and Development Authority, a unit within the U.S. Department of Health and Human Services – gave Sanofi \$43.2 million "for phase II development and manufacturing" of the Zika vaccine, according to a Sanofi press release.

KEI communications and research associate Zack Struver explained that if approved, Sanofi will also earn a priority review voucher from the U.S. Food and Drug Administration, which it could "sell on for millions of dollars," and so already has "sufficient incentive" to develop the vaccine with or without the exclusive license, he said.

Priority review vouchers are designed to speed up the review process for new drug products and thus incentivize drug companies to work to develop treatments for rare diseases or those without a robust market. Vouchers are transferable and have been sold to other companies for upwards of \$300 million.

However, the statement from the U.S. Army said there was a strong case for granting Sanofi exclusive rights to the technology, due to competition from the "many" groups working on a Zika vaccine. Sanofi is taking on "risk" by accruing the license since there is a "long way to go in terms of time and money" before a Zika vaccine can be approved, they said. Furthermore, the army is also yet to receive the patent

from the U.S. Patent and Trademark Office, and there is a chance it "may never issue," adding more "risk" for Sanofi.

"The federal government needs a non-federal partner with the research and production capabilities and the willingness to invest their own substantial funding to most quickly get this product to the market and available for public use," the spokesperson added.

The KEI letter to the army also asks for four conditions to be imposed on the licensing agreement. These include requiring Sanofi to limit the price of the vaccine to "no more than the median price being charged in other high income countries;" limiting the length of time that Sanofi has exclusive rights to the technology, requiring the vaccine be made "available and affordable" in developing countries; and requiring Sanofi to be transparent about the costs of research and development.

The U.S. Army responded by saying the license agreement has stipulations in place to "protect the public interest," including the option to terminate if Sanofi fails to "bring the invention to practical application within a reasonable time," or "make the benefits of the invention reasonably accessible to the public."

Sanofi says no "clear path to commercialization" for Zika at this time

The pharmaceutical company says that even with the public funding from BARDA, taking ZP IV through the many stages of testing, approval and manufacturing requires Sanofi to take on "financial and opportunity risks" due to the fact Zika is "still a moving target" and there is "no clear path to commercialization at this time," according to Heinrichs, Sanofi's research and development project lead.

"We have modeled various commercial scenarios including current endemic areas, spread to other geographies and the travel market, among others. The nature of the epidemiology and spread of the virus will impact the degree of profitability," Heinrichs said.

Sanofi may have a point, according to Paul Wilson, assistant professor of clinical population and family health at Columbia University's Mailman School of Public Health, who says there is "genuine uncertainty" surrounding how big the Zika problem will be and how widely a vaccine would be used. This is compounded, he said, by the fact that the virus could ultimately become widespread but "without causing harm," or even die out as people become immune.

If this turns out to be the case, however, MSF's and KEI's concerns may be valid since Sanofi would likely lose interest in the project and fail to drive the vaccine all the way through development, Wilson said.

"I'm sympathetic to MSF's position - when you have a vaccine being developed with public funding and you give the rights to one firm, you have every right to put in place conditions to make sure vaccine will be available to all who need it," he said.

"The U.S. government has to at least justify why an exclusive license is necessary," Wilson added.

Sanofi could be the best company for the job

The company has experience with vaccines against viruses in the same family as Zika, known as flaviviruses, having developed vaccines for Japanese encephalitis and dengue fever.

This could explain why the U.S. Army is keen to entrust the Zika virus vaccine to Sanofi, which is an established player and one with a track record of supplying vaccines to developing countries, according to Wilson.

"It is still more or less true that only the big multinational pharmaceutical companies have ever been able to successfully bring a truly new vaccine to market. Even when you have a vaccine candidate that's at the stage of this Zika one is now, there are still many challenges involved in the later stages of development," he said.

However, the capacity of pharmaceutical firms in India, Brazil and China to develop vaccines is "growing rapidly" and some of these firms could probably bring the vaccine to market, although perhaps not as rapidly as a multinational, Wilson said.

The vaccine industry has long been dominated by four major multinational pharmaceutical companies - GlaxoSmithKline, Merck, Sanofi-Pasteur, and Pfizer, which accounted for approximately 86 percent of global vaccine revenue in 2015. Their monopoly is attributed to entry barriers such as high start-up costs and long lead times; vaccines can take anywhere from 10 to 16 years to reach the market, preventing other companies from competing.

Phase III trials are technically difficult to conduct and many drugs and vaccines fail them, and developing a robust manufacturing process is "very technical" and is subject to "stringent regulatory requirements," which can be hard to navigate, Wilson explained.

"The U.S. Army may want a MNC partner because they believe that is the surest way to ensure that the vaccine gets developed quickly. There are only a few companies out there that have the relevant experience and have shown an active interest in developing country markets, which Sanofi has demonstrated," he said.

Access will not be an issue in the poorest countries if GAVI steps in

In relation to MSF's and KEI's concerns about access to the vaccine, if approved, GAVI, the Vaccine Alliance – a partnership of major donors and pharmaceutical companies designed to ensure access to vaccines for children in developing countries – could support low-income countries in purchasing the vaccine, Wilson said.

Sanofi confirmed in an email to Devex that it has worked with GAVI on distribution of vaccines in the past, and so working with the alliance on the Zika vaccine was “certainly a possibility,” but that a strategy for “pricing and distribution” would be developed later in the process.

However, the real problem of access will be in middle-income countries, such as Brazil, which are ineligible for GAVI funding but where the vaccine is urgently needed.

“Sanofi doesn't see a market in the poorest countries and so they're happy to provide vaccines at a reasonable price there through GAVI, since it would be seen as bad PR not to. But they are not necessarily prepared to make those concessions in places like Brazil and India, where the greatest access concerns would be,” Wilson said.

Sanofi has bad track record when it comes to serving developing countries, MSF says

MSF spoke out against Sanofi in 2015 after the company decided to stop manufacturing a pan-African snakebite antivenom because it was no longer lucrative, leaving a gap in supplies that MSF said would be likely to lead to unnecessary deaths.

The NGO is worried that if given the exclusive license for the Zika vaccine, the pharmaceutical company will follow the same path and neglect countries with great need but less opportunities for profit, according to Judit Rius Sanjuan, MSF's U.S. access campaign manager.

Instead, Sanjuan wants the U.S. Army to offer Sanofi a nonexclusive license, which she argued would be “better public policy,” ensure the Zika virus has broader geographical scope, and protects the U.S. government from “having all its apples in one basket.”

There are other ways to get medicines through development and into markets

There have been successful examples of the U.S. government offering nonexclusive licenses for patented technologies through the United Nations backed Medicines Patent Pool, a global health financing mechanism set up in 2010 to share drug technology and research to speed up development, lower costs and increase access to newer HIV/AIDS, viral hepatitis C, and tuberculosis treatments in developing countries.

MPP works by signing agreements with patent holders – such as the NIH and the U.S. Army but also nonprofits, pharmaceutical companies and individuals – to create a pool of relevant patents. The partners are then licensed to generic drug manufacturers who can then produce generic versions of the medicines, often utilizing more than one patented technology in the process of development.

For example, in 2010, the NIH licensed a patent on Darunavir to the MPP, which spurred the development of a new combination drug. Furthermore, Johns Hopkins University announced on Jan. 25 that it is licensing its patent for the drug candidate sunitinib, which could be used to treat tuberculosis, exclusively to the MPP.

While the MPP does not currently work on vaccines, and so licensing to the MPP was not an option for the U.S. Army, these examples set a “good precedent” for “innovative” nonexclusive licensing agreements and how effectively sharing research can expedite research and development, increase collaboration, and diversify the medicine development process, MSF's Sanjuan said.

Furthermore, there have been other notable examples of the U.S. granting nonexclusive licenses for the development of vaccines. For example, the human-bovine rotavirus vaccine technology was licensed by the NIH to eight organizations, one in the United States and seven in the developing countries, to manufacture and distribute the rotavirus vaccine.

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Zack Struver, Communications and Research Associate Knowledge Ecology International
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Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 9/25/2018 2:16:22 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Merritt, William (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=33aed7eef02943408617245830eb07a8-merrittw]
Subject: FW: James Douglas Griffin; CA066996

Bill and Mark:

b4, b5

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 24, 2018 3:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: James Douglas Griffin; CA066996

The first publication: <http://www.bloodjournal.org/content/early/recent>

From: Merritt, William (NIH/NCI) [E]
Sent: Thursday, September 20, 2018 2:53 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Hi Ann,

b4, b5

b4,b5

Bill

William D. Merritt, Ph.D.

Program Director

Clinical Investigations Branch

Cancer Therapy Evaluation Program

Division of Cancer Treatment and Diagnosis

National Cancer Institute

Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]

Sent: Monday, September 17, 2018 10:15 AM

To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>

Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

Subject: RE: James Douglas Griffin; CA066996

Good Morning: I just sent an outlook invite for 2:00 this Thursday, September 20th. I will link both of you. Just send me your telephone number.

Thanks for your assistance.

Ann

From: Merritt, William (NIH/NCI) [E]

Sent: Monday, September 17, 2018 9:48 AM

To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: RE: James Douglas Griffin; CA066996

Yes, I am free at various times on Thursday; unsure about about AM right now, awaiting an agenda; but around 2 is good, also 4?

Bill

From: Hammersla, Ann (NIH/OD) [E]

Sent: Monday, September 17, 2018 8:07 AM

REL0000024460

To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: James Douglas Griffin; CA066996

Good Morning Bill: Would Thursday 9/20 be better for you? I am open most of the day. Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Thursday, September 13, 2018 4:10 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

I have a full afternoon on Tuesday with meetings until 6, and Wednesday afternoon I am booked until 4, but would be available at that time (4 – 6 time frame) for this call. b4,b5

b4,b5

Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Thursday, September 13, 2018 3:53 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: James Douglas Griffin; CA066996

Hello Bill:

We are at the final stages of NIH's review of the NIH funded grants and the inventions for Rydapt. b4,b5

b4,b5

It would be helpful if you, Mark Rohrbaugh (who assists in similar requests from OSP) and you discuss the NCI grants and the results with the testing of the compounds.

Are you available next week? Would Tuesday, September 18 after 3 or Wednesday after1 be convenient? If not can you suggest another time. The discussion is intended to identify the distinctions, if any, between NIH funding, and the actual results of the testing of the named compounds.

Thank you again for your assistance.

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Wednesday, July 11, 2018 11:50 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann - I checked the P01 again,

b4, b5

Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program

REL0000024460

Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, July 11, 2018 10:59 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Morning Bill:

I have a follow-up question for you:

b4, b5

Thank you again for your assistance.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, July 09, 2018 6:08 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Good Morning Bill:

Thank you for your detailed analysis. I will keep you updated on the next steps.

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Friday, July 06, 2018 7:58 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann –

I'm very sorry for the delay in responding, but finally now today I have had a (first) chance to get to this and other long delayed work, since some regular meetings were canceled.

REL0000024460

b4,b5

Regards,
Bill Merritt

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, June 25, 2018 10:57 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Bill:

Do you have any questions regarding your review of CA066996?

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Monday, May 21, 2018 3:06 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

Thanks for this instructive drill down for explanation of these terms, important in my review of this issue.

Will be in touch,
Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

REL0000024460

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, May 21, 2018 2:36 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Dear Bill:

Thank you for taking your time today to discuss CA066996 and if the supported research was used for the conception or reduction of Rydapt.

The definition of "subject invention" that is defined by the Bayh-Dole statute and regulation is: "any invention of the contractor conceived for first actually reduced to practice in the performance of work under this contract...."

"Conception" and "first actually reduced to practice" is not defined in the Bayh-Dole statute. The following are definitions taken from the patent examiner's procedure manual or a law firm specializing in patent law.

"Conception" is defined in the patent examiner's procedures as "the complete performance of the mental part of the inventive act" and it is "the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is thereafter to be applied in practice...."

Another definition of "Conception" from a law firm:

Conception is the touchstone of inventorship, the completion of the mental part of invention. It is "the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation.

The patent examiner's procedures defined "reduction to practice" as

Reduction to practice may be an actual **reduction** or a constructive **reduction to practice** which occurs when a patent application on the claimed invention is filed. The filing of a patent application serves as conception and constructive **reduction to practice** of the subject matter described in the application.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 3:23 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Dear Bill:

I have attached the KEI request for NIH to take title or other actions to the patents in question. I have also attached Dana Farber's response and 3 citations to publications (2 have abstracts) that link Dr. Griffin's funding on two publications to CA066996. I have also identified over 100 other publications that are being reviewed.

I will send you an outlook meeting time for Monday. Thank you again for your assistance.

REL0000024460

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Tuesday, May 15, 2018 11:33 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

I am leaving town very soon to attend a conference the rest of the week. So next Monday morning would be the first opportunity to talk. It may be helpful to send the information as background to me so I can look it over before we speak.

Best regards,
Bill Merritt

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 11:17 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: James Douglas Griffin; CA066996

Dear Dr. Merritt:

NIH received a request from Knowledge Ecology International (KEI) requesting NIH to take multiple actions, including, taking title to certain patents filed by the Dana Farber Institute for inventions made by Dr. James Douglas Griffin that have led to the therapeutic Rydapt®. According to QVR you are listed as the PO for the above grant that Dr. Griffin is supported on. In order to respond to the KEI request an understanding and information is needed to determine if there is a link between Dr. Griffin's NIH funding and the development of this therapeutic. Rydapt® is used for the treatment of acute myeloid leukemia, myelodysplastic syndrome and advanced systemic mastocytosis. There are 2 patents that Dr. Griffin is identified as an inventor that the FDA reports are used in the commercialization of Rydapt®. Both of the patents' abstracts state:

The present invention relates to the use of staurosporines derivatives for the preparation of a drug for the treatment of diseases involving deregulated FLT3 receptor tyrosine kinase activity, especially for the curative and/or prophylactic treatment of leukemias and myelodysplastic syndromes, and to a method of treating diseases involving deregulated FLT3 receptor tyrosine kinase activity.

Before sending you additional background information you may need to identify the issues that have been raised, it may be helpful if we talked first. Or, if you prefer I can forward you the information received by KEI and the summaries prepared thus far for your review.

Please let me know when you are available for a 30 minute discussion. If it helps I am available this Thursday or Friday afternoon and Monday May 21 in the morning. Let me know if you would like to receive the background information before we talk.

Thank you in advance for your assistance.

Ann

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REL0000024460

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 4/20/2018 11:42:28 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: KEI Letter to HHS Secretary Azar on Exondys 51
Attachments: James Love letter-KEI-Exondys 51_4.19.2018.pdf

FYI

From: Jackson, Stephanie (NIH/OD) [C]
Sent: Thursday, April 19, 2018 4:51 PM
To: james.love@keionline.org
Cc: admin@healthgap.org; david@patientsforaffordabledrugs.org; pfamrx@gmail.com; alawson@socialsecurityworks.org; office@essentialmedicine.org; Levinson, Dan R (OIG/IO) <dan.levinson@oig.hhs.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: KEI Letter to HHS Secretary Azar on Exondys 51

Sent on behalf of Michelle G. Bulls –

Good afternoon Mr. Love,

Attached please find, letter from the NIH in response to your letter dated April 5, 2018 to HHS Secretary Azar.

Thank you,
MGB

Stephanie G. Jackson, Executive Assistant
Contractor- Ripple Effect Communications, Inc.
Office of Policy for Extramural Research Administration, OER
NIH Office of the Director

6705 Rockledge Drive, Suite 350A
Bethesda, MD 20892-7974
Phone: 301-451-4221
Email: Stephanie.jackson3@nih.gov

REL0000024461



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

April 19, 2018

Mr. James Love
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, D.C. 20009

Sent by Email: james.love@keionline.org


Subject: KEI April 5, 2018 Letter to HHS Secretary Azar on Exondys 51

Dear Mr. Love:

The National Institutes of Health (NIH) is responding on behalf of the Department of Health and Human Services, to your April 5, 2018 request that was signed by Knowledge Ecology International (KEI) and five other organizations (KEI Request) to Secretary Azar concerning Exondys 51®. The KEI Request asked that Health and Human Services (HHS) exercise its rights under the Bayh-Dole Act to take title to five patents on eteplirsén, as a remedy to a failure by the University of Western Australia to disclose NIH funding of the inventions, and to use the ownership of those patents as leverage to obtain lower prices to Exondys 51®.

NIH is currently reviewing the information KEI provided along with NIH funding records, disclosures to NIH of any applicable inventions, the U.S. Patent and Trademark Office records, and any other relevant documents. When NIH's analysis is completed we will notify you.

Sincerely,


Michelle G. Bulls

Director

Office of Policy for Extramural Research Administration
Office of Extramural Research
National Institutes of Health

cc: Health GAP: admin@healthgap.org
Patients for Affordable Drugs: david@patientsforaffordabledrugs.org
People of Faith for Access to Medicines: pfamrx@gmail.com
Social Security Works: alawson@socialsecurityworks.org
Universities Allied for Essential Medicines: office@essentialmedicine.org
HHS OIG - Daniel R. Levinson: Dan.Levinson@oig.hhs.gov

REL0000024461.0001

From: Jambou, Robert (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=FF42A9FA39824980AA9E36AF49E56CBC-JAMBOUR]
Sent: 7/23/2018 8:27:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Jorgenson, Lyric (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3bbde7d361374981a4d336b6eeb17521-jorgensonla]
Subject: RE: KEI [Goldman] FOIA #45260

That's fine. Because BRAIN is developed internally but is used in testimony before Congress, the BRAIN records do not in whole constitute "internal communications that would only be subject to discovery under litigation" under exemption (b)(5).

As long as we can easily separate out factual information from statements of opinion or pre-decisional policy information, we are in accord with the statute.

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 4:21 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Cc: Jorgenson, Lyric (NIH/OD) [E] <lyric.jorgenson@nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 4:07 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

Let me know if this poses a problem and I will consult with the NIH FOIA officer in this regard (with approval from senior staff) if necessary.

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 3:27 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:48 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

b5

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:41 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Just wondered.

b5

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:39 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Typically not (and not if they are NIH employees). I cannot recall ever doing that.
Is there something specific?

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 2:35 PM
To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

For released emails, would you redact names of people sending, receiving emails?

From: Jambou, Robert (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI [Goldman] FOIA #45260

Done – I added the incoming request to the TTIP FOIA folder – see page 2 (blue highlight).

Bob J.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, July 23, 2018 12:36 PM

REL0000024465

To: Jambou, Robert (NIH/OD) [E] <jambour@od.nih.gov>

Subject: RE: KEI [Goldman] FOIA #45260

Will do. Can you remind me what the request was exactly?

From: Jambou, Robert (NIH/OD) [E]

Sent: Monday, July 23, 2018 12:32 PM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Subject: KEI [Goldman] FOIA #45260

Hi Mark,

I have finished the review of the KEI March-In Petition FOIA.

There are 322* responsive .pdf files (including attachments) for your QC review.

To facilitate the task, I have divided the responsive categories into 3 types:

b5

If you could take a look at these files, I would appreciate it (especially the ones labeled "Check or muCheck". If you have comments, please use the Adobe comment tool and add your initials to the end of the file so I can spot those quickly.

I have created a folder and copied the responsive files here into three different sub-folders according to

status: [J:\TTIP\KEI Goldman FOIA 45260](#)

Happy to help you with this. Let me know

b5

Regards,

Bob J.

From: Koniges, Ursula (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D5AE2C3139654BC0B9B95718D516310B-KONIGESUM]
Sent: 1/10/2019 10:17:34 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Drug Pricing & Secretary Azar
Attachments: Drug Pricing - TTIP Reviewed - clean.docx

Hi Mark,

If the attached document seems ready to you, I'll go ahead and put this in the folder for Lyric's review. The following further updates are included in the attached document (tracked changes accepted, highlights left to indicate new content):

b5

Thanks,
-Ursula

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 4:37 PM
To: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Subject: RE: Drug Pricing & Secretary Azar

Looks good.

b5

b5

From: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Sent: Thursday, January 10, 2019 4:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Drug Pricing & Secretary Azar

Hi Mark,

I've gotten the

b5

b5

Thanks,
-Ursula

From: Koniges, Ursula (NIH/OD) [E]
Sent: Thursday, January 10, 2019 4:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: Drug Pricing & Secretary Azar

I've added the following bullet to the

b5

b5

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 4:07 PM
To: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Subject: RE: Drug Pricing & Secretary Azar

I would put it in the b5

b5

From: Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>
Sent: Thursday, January 10, 2019 4:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Drug Pricing & Secretary Azar

Hi Mark, quick FYI b5

Azar Says He And Trump Are Determined To Reduce Prescription Drug Prices.

On Fox Business' Varney & Co. (1/9, 198K), HHS Secretary Alex Azar was interviewed about the fact that manufacturers recently raised prescription drug prices, hindering President Trump's efforts to lower them. Azar said, "I want to be really clear to pharma companies out there and to pharmacy benefit managers: the President and I will not stop until list prices of drugs come down. This behavior has to stop, drug prices must come down and we will roll out more regulatory and legislative proposals and we will work with Democrats and Republicans to get drug prices down." Asked about criticism that the President is attempting to institute drug price controls, Azar stated, "The companies that increased their prices...on January 1 all admitted they were doing so basically to funnel kickbacks in the form of rebates to pharmacy benefit managers to keep preferred status of their drugs on the formularies available to patients. Now we've seen some good behavior: you know Amgen, Merck, Gilead, each of them have products" whose list prices "they have significantly reduced." Azar said, "We need to see more of this, we need other companies to follow, we need bigger products to have those price decreases." Fox Business (1/9, Limitone, 1.55M) also reports on the interview.

In Tweets, Azar Demands That Manufacturers Lower Prescription Drug Prices.

BioPharma Dive (1/9, Dunn) reports that drugmakers "largely reverted to boosting list prices in January even after a year of criticism from the Trump administration and some companies pledging to hold off. The White House is now weighing in with Health and Human Services Secretary Alex Azar threatening further regulatory and legislative action if list prices do not come down." On Wednesday, "Azar put the industry and pharmaceutical benefit managers, or PBMs, on blast with a tweet thread...capped off with a cable news hit." Health Exec (1/9, Baxter) reports that Azar tweeted, "Prices must start coming down." But "the message – which was published a day after Trump called a meeting with White House officials on the issue – didn't come with any new proposals or plans from the agency he leads. The Twitter action also comes a day before Democrats in Congress plan to introduce a legislative package to 'drastically' reduce drug prices."

Columnist: Azar's Tweets Show Trump Administration Is Not Happy With Drug Price Hikes.

Max Nisen writes in a Bloomberg View (1/9, 5.74M) column that after raising prices on January 1, "drug executives followed up this week with less-than-contrite messaging at" the J.P. Morgan Chase & Co. Healthcare Conference, "signaling the industry's reluctance to change in the face of constant criticism." Nisen says the Trump Administration is displeased with the price increases. On Tuesday, President Trump "reportedly summoned advisers to meet on the issue, and on Wednesday, Health and Human Services Secretary Alex Azar launched a tweet storm to take the sector [to task] for its lack of progress."

b5

b5

b5

b5

b5

From: Joe Allen [jallen@allen-assoc.com]
Sent: 5/15/2019 9:04:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Jamie Love's response to Fred Reinhart and NIH CRADAS

His response to Fred's earlier column just went up:
<https://www.ipwatchdog.com/2019/05/15/jamie-love-responds-criticism-knowledge-ecology-international-letter/id=109239/>

Note his critique of the decline in NIH CRADAS per the reasonable pricing clause as well as his claims on government investment in several drugs. Worth mulling over how to respond.

--

Joseph P. Allen
President
Allen and Associates
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Bethesda, OH 43719
(W) 740-484-1814
(C) [REDACTED] b6
www.allen-assoc.com

From: Joe Allen [jallen@allen-assoc.com]
Sent: 10/6/2017 1:55:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

<http://www.keionline.org/node/2867>

KEI asks HHS to use Bayh-Dole rights in Zinbryta patent (drug for multiple sclerosis)

Submitted by KEI Staff on 14. September 2017 - 12:30

- Medical Technologies

Attached is a letter sent on September 14, 2017 to Andrew Bremberg, an Assistant to the President and the Director of the Domestic Policy Council at the White House, and Keagan Lenihan, a Senior Adviser to HHS Secretary Tom Price, regarding Zinbrytra (INN: daclizumab), a drug to approved by the FDA to treat multiple sclerosis. (PDF version [here](#))

This is an older drug, and the NIH obtained a patent on its use to treat multiple sclerosis, and licensed the patent on a exclusive basis to Biogen. Biogen and Abbvie market the drug around the world. The price in the United States is more than \$96,000 per year (\$7390 per injection every 4 weeks, 13 times a year), but far lower in every high income country where KEI obtained prices.

The letter asks DHHS to use one or more of three federal rights in the NIH licensed patent to "authorize affordable competition, or to force Biogen to lower its price." The three actions include using the royalty free right in the patent, exercising march-in rights, or terminating the license. The option to terminate the license is featured in the letter, and it is an action that KEI had not focused on previously.

The termination clause is something the U.S. government can do with government owned patents, including any owned by the NIH.

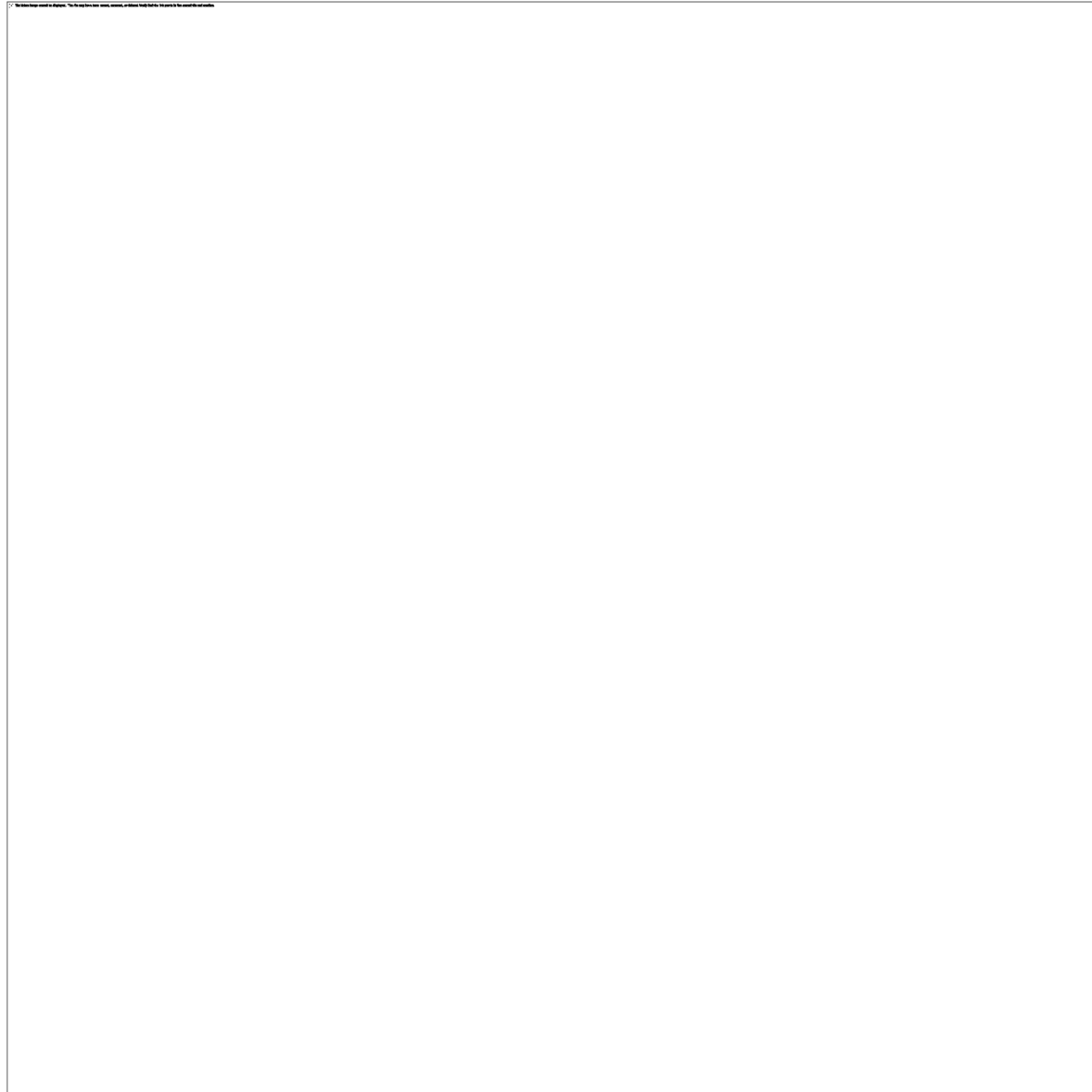
At the end of this blog is a graph of the prices of MS drugs, over time.

Below is an excerpt from the beginning and another excerpt from the end of the letter.

We write to you today with regard to the excessive price of an important drug for multiple sclerosis called daclizumab, co-marketed by Biogen and AbbVie as Zinbryta at prices roughly 3 to 4 times higher in the United States than in other high income countries. The patent for Zinbryta was licensed from the NIH, and under the Bayh-Dole Act there are three specific actions the United States government can and should utilize to authorize affordable competition, or to force Biogen to lower its price. These include: (1) making use of the government's royalty-free rights in the patent; (2) utilizing the "march-in" right to license the patent to a third party; and/or (3) terminating the exclusive license.

Amidst a crisis of out-of-control drug prices, this is an instance where the federal government has the power to act without the need for any additional statutory authority.

[snip]



[snip]

The United States prices are 2.8 to 4.3 times higher than any of the reference countries. The U.S. price is 2.8 times higher than Norway and Denmark and 3.8 times higher than Switzerland, even though all three of these countries have higher per capita incomes than the United States, and the U.S. taxpayers funded the relevant discovery and own the patent.

There is no reason to accept a foreign price, even from a country of a similar per capita income, as reasonable. But in our opinion, it is unreasonable for Biogen/Abbvie to charge higher prices in

the United States than in other large economies with a per capita income at least 50 percent of the United States.

In this case, prices in the U.S. are not only higher — they are 180 to 330 percent higher than every high income country where KEI could obtain pricing data. The pricing of Zinbryta is contrary to statutory requirement of the Bayh-Dole Act to make the inventions available to the public on reasonable terms.

A failure by HHS to address the discrimination against U.S. residents in pricing harms everyone who buys or reimburses the drugs, including all U.S. taxpayers, all employers who pay for health benefits, and many persons living with multiple sclerosis who face daunting co-payments, who are underinsured, or who never get the drug because of its high cost.

Conclusion

We request that the Department of Health and Human Services use one or more of the three options at its disposal under the Bayh Dole Act to lower prices of this important MS drug, including:

- (1) under 35 U.S.C. § 209(d)(1), utilizing the royalty-free license in the government-owned patent to authorize generic competition;
- (2) under 35 U.S.C. § 203(a), utilizing the “march-in” rights to license the drug to a third party; or
- (3) 35 U.S.C. § 209(d)(3), terminating the exclusive NIH license to Abbott/Biogen on the ground that the company is failing to abide by its obligation to make to invention “available to the public on reasonable terms”.

Specifically, this letter should be seen as request to exercise march-in rights under 35 U.S.C. § 203(a), and/or to terminate the license under 35 U.S.C. § 209(d)(3), on the grounds that charging U.S. residents 2.8 to 4.3 times more than residents in other high income countries is on its face unreasonable, and in violation of the requirement in 35 U.S.C. § 201(f) to make the invention covered by the license “available to the public on reasonable terms.” We also urge DHHS to use the royalty-free right in the patents to exercise leverage and freedom to operate whenever it faces challenges in implementing its section 203 or 209 rights.

We believe that terminating the exclusive license may be the best option, because it will provide the most leverage and the most flexibility in terms of obtaining alternative supplies of the product. But a credible threat to use any of these three options will be sufficient to force Biogen and AbbVie to lower its price of Zinbryta, at least to the prices that the companies already charge in other countries with incomes similar to the United States.

The Trump Administration has made numerous public pronouncements regarding the need to fight high drug prices, a policy point supported by overwhelming public opinion. In this instance, the government has all of the leverage it needs to take strong, decisive action to benefit multiple sclerosis patients, consumers, and taxpayers.

We request a meeting at your earliest convenience to discuss this matter further.

Attachment

Size

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/21/2018 12:25:12 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Rydapt - failure to disclose federal funding
Attachments: ANNEX-KEI-Briefing-Note-2018-1.pdf; ANNEX-griffin-CA36167-NIH-REPORTER.pdf; ANNEX-james-griffin-NIH-RePORTer-20March2018.pdf; Rydapt-james-griffin-dana-farber-novartis-21Mar2018.pdf; AnnHammersla-Rydapt-20March2018.pdf

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]
Sent: Wednesday, March 21, 2018 8:09 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: Re: Rydapt - failure to disclose federal funding

Dear Ann:

Thank you for your reply. Attached please find five pdf documents concerning the Rydapt issue I mentioned yesterday:

- (1) a brief cover letter regarding the Rydapt issue;
- (2) the memorandum on the failure to disclose (Rydapt-james-griffin-dana-farber-novartis-21Mar2018);
- (3) ANNEX: James Griffin's 71 NIH Funded Projects (ANNEX-james-griffin-NIH-RePORTer-20March2018);
- (4) ANNEX: Griffin's CA36167 Grants, from NIH REPORTER (ANNEX-griffin-CA36167-NIH-REPORTER)
- (5) ANNEX: KEI-Briefing-Note-2018-1

Thank you for your attention to this matter.

Sincerely,
Andy

--
Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

On Tue, Mar 20, 2018 at 3:27 PM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

Dear Andrew:

Thank you for your courtesy notice that KEI is submitting a new request asking the NIH to take ownership actions for Rydapt.

NIH will review the Rydapt request and NIH's funding, if any, and is now reviewing the earlier requests you have submitted and will you and KEI know the results of NIH's internal research.

Ann

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

From: Andrew Goldman <andrew.goldman@keionline.org>

Sent: Tuesday, March 20, 2018 1:22 PM

To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

Cc: Jamie Love <james.love@keionline.org>

Subject: Rydapt - failure to disclose federal funding

Dear Dir. Hammersla:

I wanted to provide you a courtesy notice that we are finalizing a document similar to the two we have sent in recent days, this time requesting that NIH conduct an investigation into the failure to disclose federal funding leading to the expensive medicine Rydapt (INN midostaurin). The document requests that NIH remedy that failure by taking title to the patents at issue. The memorandum and appendices will detail the grants issued to inventor James Griffin, and their relationship to the patents.

Kind regards,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

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Search in: Projects Admin IC: All, Principal Investigator / Project Leader: griffin, james, Project Number:%36167%, Fiscal Year: All Fiscal Years

Click on the column header to sort the results

T: Application Type; Act: Activity Code; Project: Admin IC, Serial No.; Year: Support Year/Supplement/Amendment

	T	Act	Project	Year	Sub #	Project Title	Contact PI/ Project Leader	Organization	FY	Admin IC	Funding IC	FY Total Cost by IC	Similar Projects
	5	R01	CA036167	02		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1985	NCI	NCI	\$127,387	
	5	R01	CA036167	03		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1986	NCI	NCI	\$116,972	
	2	R01	CA036167	04		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1987	NCI	NCI	\$155,176	
	5	R01	CA036167	05		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1988	NCI	NCI	\$160,132	
	5	R01	CA036167	06		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1989	NCI	NCI	\$171,325	
	2	R01	CA036167	07		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1990	NCI	NCI	\$231,707	
	5	R01	CA036167	08		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1991	NCI	NCI	\$227,031	
	5	R01	CA036167	09		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1992	NCI	NCI	\$239,969	
	5	R01	CA036167	10		SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1993	NCI	NCI	\$256,211	
	5	R01	CA036167	11		SURFACE ANTIGENS OF MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1994	NCI	NCI	\$246,082	
	2	R37	CA036167	12		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1995	NCI	NCI	\$257,305	
	5	R37	CA036167	13		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1996	NCI	NCI	\$265,333	
	5	R37	CA036167	14		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1997	NCI	NCI	\$279,107	
	5	R37	CA036167	15		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1998	NCI	NCI	\$282,790	
	5	R37	CA036167	16		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1999	NCI	NCI	\$296,957	
	4	R37	CA036167	17		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2000	NCI	NCI	\$278,098	
	5	R37	CA036167	18		REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2001	NCI	NCI	\$286,296	

<input type="checkbox"/>	5	R37	CA036167	19	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2002	NCI	NCI	\$298,972	
<input type="checkbox"/>	2	R01	CA036167	20	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2003	NCI	NCI	\$355,929	
<input type="checkbox"/>	5	R01	CA036167	21	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2004	NCI	NCI	\$355,929	
<input type="checkbox"/>	5	R01	CA036167	22	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2005	NCI	NCI	\$355,929	
<input type="checkbox"/>	5	R01	CA036167	23	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2006	NCI	NCI	\$347,565	
<input type="checkbox"/>	5	R01	CA036167	24	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2007	NCI	NCI	\$337,486	

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	5	R01	CA036167	02	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1985	NCI	NCI	\$127,387	
	5	R01	CA036167	03	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1986	NCI	NCI	\$116,972	
	2	R01	CA036167	04	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1987	NCI	NCI	\$155,176	
	1	R01	CA047843	01	REGULATION OF CSF PRODUCTION BY NORMAL HUMAN CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1988	NCI	NCI	\$107,337	
	5	R01	CA036167	05	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1988	NCI	NCI	\$160,132	
	5	R01	CA036167	06	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1989	NCI	NCI	\$171,325	
	5	R01	CA047843	02	REGULATION OF CSF PRODUCTION BY NORMAL HUMAN CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1989	NCI	NCI	\$158,079	
	2	R01	CA036167	07	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1990	NCI	NCI	\$231,707	
	5	R01	CA047843	03	REGULATION OF CSF PRODUCTION BY NORMAL HUMAN CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1990	NCI	NCI	\$151,032	
	1	R01	DK043904	01	G1/S CELL CYCLE CONTROL IN HUMAN HEMATOPOIETIC CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1991	NIDDK	NIDDK	\$241,232	
	5	R01	CA036167	08	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1991	NCI	NCI	\$227,031	
	5	R01	CA036167	09	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1992	NCI	NCI	\$239,969	
	5	R01	DK043904	02	G1/S CELL CYCLE CONTROL IN HUMAN HEMATOPOIETIC CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1992	NIDDK	NIDDK	\$245,950	
	5	R01	CA036167	10	SURFACE ANTIGENS OF HUMAN MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1993	NCI	NCI	\$256,211	
	5	R01	DK043904	03	G1/S CELL CYCLE CONTROL IN HUMAN HEMATOPOIETIC CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1993	NIDDK	NIDDK	\$269,282	
	5	R01	CA036167	11	SURFACE ANTIGENS OF MYELOID PROGENITOR CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1994	NCI	NCI	\$246,082	
	5	R01	DK043904	04	G1/S CELL CYCLE CONTROL IN HEMATOPOIETIC CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1994	NIDDK	NIDDK	\$266,012	

2	R37	CA036167	12	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1995	NCI	NCI	\$257,305
5	R01	DK043904	05	G1/S CELL CYCLE CONTROL IN HEMATOPOIETIC CELLS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1995	NIDDK	NIDDK	\$276,652
1	P01	CA066996	01A1	NOVEL THERAPEUTIC STRATEGIES IN LEUKEMIA AND LYMPHOMA	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1996	NCI	NCI	\$2,004,678
1	R01	CA070910	01	ACTIVATION OF SIGNAL TRANSDUCTION PATHWAYS BY BCR/ABL	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1996	NCI	NCI	\$264,038
5	R37	CA036167	13	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1996	NCI	NCI	\$265,333
1	P01	CA066996	02	0002 DEVELOPMENT OF IMMUNOTHERAPIES FOR CHRONIC MYELOID LEUKEMIA	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1997	NCI		\$221,144
1	P01	DK050654	02	0002 SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1997	NIDDK		\$210,597
5	P01	CA066996	02	NOVEL THERAPEUTIC STRATEGIES IN LEUKEMIA AND LYMPHOMA	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1997	NCI	NCI	\$1,990,293
5	R37	CA036167	14	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1997	NCI	NCI	\$279,107
1	P01	CA066996	03	0002 DEVELOPMENT OF IMMUNOTHERAPIES FOR CHRONIC MYELOID LEUKEMIA	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1998	NCI		\$228,568
3	P01	DK050654	03S1	0002 SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1998	NIDDK		\$198,808
5	P01	CA066996	03	NOVEL THERAPEUTIC STRATEGIES IN LEUKEMIA AND LYMPHOMA	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1998	NCI	NCI	\$2,057,110
5	P01	DK050654	03	0002 SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1998	NIDDK		\$198,808
5	R37	CA036167	15	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1998	NCI	NCI	\$282,790
7	P50	HL054785	04	0003 GENE TRANSDUCTION INTO HUMAN HEMATOPOIETIC STEM CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1998	NHLBI		\$266,789
5	P01	CA066996	04	0002 DEVELOPMENT OF IMMUNOTHERAPIES FOR CHRONIC MYELOID LEUKEMIA	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1999	NCI		\$226,134
5	P01	CA066996	04	NOVEL THERAPEUTIC STRATEGIES IN LEUKEMIA AND LYMPHOMA	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1999	NCI	NCI	\$2,035,202
5	P01	DK050654	04	0002 SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1999	NIDDK		\$198,808
5	P50	HL054785	05	0003 GENE TRANSDUCTION INTO HUMAN HEMATOPOIETIC STEM CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	1999	NHLBI		\$266,789
5	R37	CA036167	16	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	1999	NCI	NCI	\$296,957
4	R37	CA036167	17	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2000	NCI	NCI	\$278,098
5	P01	CA066996	05	0002 DEVELOPMENT OF IMMUNOTHERAPIES FOR CHRONIC MYELOID LEUKEMIA	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	2000	NCI		\$226,134
5	P01	CA066996	05	NOVEL THERAPEUTIC STRATEGIES IN LEUKEMIA AND LYMPHOMA	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2000	NCI	NCI	\$2,102,745
5	P01	DK050654	05	0002 SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	2000	NIDDK		\$148,636
5	P01	CA066996	05A1	NOVEL THERAPEUTIC STRATEGIES	GRIFFIN, JAMES	DANA-FARBER	2004	NCI	NCI	\$222,847

	2 P01 CA036167 0001	IN LEUKEMIA AND LYMPHOMA	DOUGLAS	CANCER INSTITUTE	2001	NCI	NCI	\$932,941	
	3 P01 DK050654 05S1 0002	SIGNAL TRANSDUCTION PATHWAYS IN STABLE PHASE CHRONIC MYELOID LEUKEMIA CELLS	GRIFFIN, JAMES D	DANA-FARBER CANCER INSTITUTE	2001	NIDDK		\$296,752	
	5 R37 CA036167 18	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2001	NCI	NCI	\$286,296	
	5 R37 CA036167 19	REGULATION OF MYELOPOIESIS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2002	NCI	NCI	\$298,972	
	2 R01 CA036167 20	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2003	NCI	NCI	\$355,929	
	5 R01 CA036167 21	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2004	NCI	NCI	\$355,929	
	5 R01 CA036167 22	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2005	NCI	NCI	\$355,929	
	5 R01 CA036167 23	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INSTITUTE	2006	NCI	NCI	\$347,565	
	5 R01 CA036167 24	REGULATION OF HEMATOPOIESIS BY NOTCH RECEPTORS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2007	NCI	NCI	\$337,486	
	2 P01 CA066996 11A1 0008	TYROSINE KINASE ONCOGENES IN ACUTE MYELOID LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2008	NCI		\$302,258	
	5 P01 CA066996 12 0008	TYROSINE KINASE ONCOGENES IN ACUTE MYELOID LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2009	NCI		\$311,047	
	5 P01 CA066996 12	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2009	NCI	NCI	\$2,367,210	
	5 P01 CA066996 13 0008	TYROSINE KINASE ONCOGENES IN ACUTE MYELOID LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2010	NCI		\$315,567	
	5 P01 CA066996 13	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2010	NCI	NCI	\$2,408,966	
	5 P01 CA066996 14 0008	TYROSINE KINASE ONCOGENES IN ACUTE MYELOID LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2011	NCI		\$298,834	
	5 P01 CA066996 14	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2011	NCI	NCI	\$2,306,268	
	5 P01 CA066996 15 0008	TYROSINE KINASE ONCOGENES IN ACUTE MYELOID LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2012	NCI		\$300,681	
	5 P01 CA066996 15	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	GRIFFIN, JAMES DOUGLAS	DANA-FARBER CANCER INST	2012	NCI	NCI	\$2,324,734	
	2 P01 CA066996 16A1 7129	SAMPLE PROCESSING AND ANALYSIS CORE	GRIFFIN, JAMES DOUGLAS	BRIGHAM AND WOMEN'S HOSPITAL	2014	NCI		\$280,536	
	2 P01 CA066996 16A1 7142	CLINICAL RESEARCH SUPPORT CORE	STONE, RICHARD M et al.	BRIGHAM AND WOMEN'S HOSPITAL	2014	NCI		\$293,743	
	2 P01 CA066996 16A1	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	EBERT, BENJAMIN LEVINE et al.	BRIGHAM AND WOMEN'S HOSPITAL	2014	NCI	NCI	\$2,307,647	
	5 P01 CA066996 17 7129	SAMPLE PROCESSING AND ANALYSIS CORE	GRIFFIN, JAMES DOUGLAS	BRIGHAM AND WOMEN'S HOSPITAL	2015	NCI		\$270,902	
	5 P01 CA066996 17 7142	CLINICAL RESEARCH SUPPORT CORE	STONE, RICHARD M et al.	BRIGHAM AND WOMEN'S HOSPITAL	2015	NCI		\$284,644	
	5 P01 CA066996 17	DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	EBERT, BENJAMIN LEVINE et al.	BRIGHAM AND WOMEN'S HOSPITAL	2015	NCI	NCI	\$2,250,582	
	5 P01 CA066996 18 7129	SAMPLE PROCESSING AND ANALYSIS CORE	GRIFFIN, JAMES DOUGLAS	BRIGHAM AND WOMEN'S HOSPITAL	2016	NCI		\$270,933	

	5	P01	CA066996	18	7142	CLINICAL RESEARCH SUPPORT CORE	STONE, RICHARD M et al.	BRIGHAM AND WOMEN'S HOSPITAL	2016	NCI		\$284,672	
	5	P01	CA066996	18		DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	EBERT, BENJAMIN LEVINE et al.	BRIGHAM AND WOMEN'S HOSPITAL	2016	NCI	NCI	\$2,249,567	
	5	P01	CA066996	19	7129	SAMPLE PROCESSING AND ANALYSIS CORE	GRIFFIN, JAMES DOUGLAS	BRIGHAM AND WOMEN'S HOSPITAL	2017	NCI		\$270,948	
	5	P01	CA066996	19	7142	CLINICAL RESEARCH SUPPORT CORE	STONE, RICHARD M et al.	BRIGHAM AND WOMEN'S HOSPITAL	2017	NCI		\$284,685	
	5	P01	CA066996	19		DEVELOPMENT OF NOVEL THERAPEUTIC STRATEGIES IN HUMAN LEUKEMIAS	EBERT, BENJAMIN LEVINE et al.	BRIGHAM AND WOMEN'S HOSPITAL	2017	NCI	NCI	\$2,248,452	

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Rydapt (INN midostaurin)
Failures to disclose government funding for patents granted to James Griffin and assigned to Dana-Farber Cancer Institute in the FDA Orange Book

Knowledge Ecology International
March 21, 2018

Table of Contents

Introduction	2
What Is Midostaurin?	2
What Does Rydapt Do?	3
The Cost of Rydapt	4
The Orange Book Patents for Rydapt	4
Table 1: The Orange Book patents for Rydapt	4
The Griffin Patents that Failed to Disclose Federal Funding	5
Table 2: The two FLT3 Griffin patents	5
The James Griffin Research Grants from the National Institutes of Health	5
NIH Grants for which James Griffin was a Principal Investigator	5
Table 3: Funding by fiscal year for 71 NIH funded projects and subprojects listing James Griffin as the principal investigator, from 1985 to 2017	6
Table 4: NIH grants from 1996 to 2001 with title: "Novel Therapeutic Strategies in Leukemia and Lymphoma."	7
Table 5: Seven papers published from 2002 to 2007 describing the role of FLT3 and PTK inhibitors for the treatment of leukemia cells.	8
Table 6: Seven DK050654 projects listing James Griffin as the PI and Dana-Farber as the institution.	10
Table 7: CA066996 grants from 2008 to 2011	10
Requested Remedies for Non-disclosure	11
Attachments:	12

Introduction

Knowledge Ecology International (KEI) asks the Department of Health and Human Services (DHHS) to investigate a failure to disclose National Institutes of Health (NIH) research funding on two patents granted to James D. Griffin as the lead inventor, and assigned to a single entity, Dana-Farber Cancer Institute.

Patents 7,973,031 and 8,222,244 are listed as the first two patents (out of three patents) in the FDA Orange Book for the drug Rydapt (INN midostaurin), used for the treatment of acute myeloid leukemia (AML), myelodysplastic syndrome and advanced systemic mastocytosis (ASM).

The cost of Rydapt depends upon the indication and patient weight. For a typical patient, the cost for the treatment of AML is \$195,405 per year, and for ASM, \$390,811 per year. In both cases, the high cost is a barrier to access and a fiscal strain on health systems.

From 1985 to 2017, James Griffin was the principal investigator for 46 projects and 25 sub projects funded by the NIH totalling \$44 million. All of the grants involve research on leukemia.

KEI is asking the NIH to take title to the patents, which is a remedy available under the Bayh-Dole Act for non-disclosure of federal funding of patented inventions. At a minimum, the Department of Health and Human Services should require the Dana-Farber Cancer Institute to correct the failure to disclose the relevant NIH grants.

What Is Midostaurin?

Midostaurin is a multi-targeted protein kinase inhibitor that was synthesized by Giorgio Caravatti in 1986,¹ originally encoded as CGP 41251 and later known as PKC421, as part of a drug discovery program aimed toward optimizing the inhibitory activity of staurosporine, a natural product isolated from *Streptomyces staurosporeus*, against protein kinase C (PKC). To investigate its potential as a PKC inhibitor, studies were conducted revealing midostaurin's ability to inhibit cell proliferation (by interfering with cell-cycle activity) and inhibit solid tumor growth (by displaying antiproliferative activity).^{2,3} Following oral administration, midostaurin

¹ Caravatti G, Meyer T, Fredenhagen A, et al. Inhibitory activity and selectivity of staurosporine derivatives towards protein kinase C. *Bioorg Med Chem Lett*. 1994;4(3):399–404.

² Ikegami Y, Yano S, Nakao K. Antitumor effect of CGP41251, a new selective protein kinase C inhibitor, on human non-small cell lung cancer cells. *Jpn J Pharmacol*. 1996;70(1):65-72.

³ Ikegami Y, Yano S, Nakao K. Effects of the new selective protein kinase C inhibitor 4'-N-benzoyl staurosporine on cell cycle distribution and growth inhibition in human small cell lung cancer cells. *Arzneimittelforschung*. 1996;46(2):201-204

produces active metabolites that target the protein kinase C family including serine-threonine and tyrosine kinases.⁴

What Does Rydapt Do?

On April 28, 2017 the FDA approved Rydapt (INN midostaurin) for the following indications:

- Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

The FDA released the following statement:⁵

“Rydapt is the first targeted therapy to treat patients with AML, in combination with chemotherapy,” said Richard Pazdur, M.D., acting director of the Office of Hematology and Oncology Products in the FDA’s Center for Drug Evaluation and Research and director of the FDA’s Oncology Center of Excellence. “The ability to detect the gene mutation with a diagnostic test means doctors can identify specific patients who may benefit from this treatment. ...The safety and efficacy of Rydapt for patients with AML were studied in a randomized trial of 717 patients who had not been treated previously for AML.”

The Dana-Farber Cancer Institute issued its own press release, titled “Backed by Dana-Farber research, FDA approves new AML drug,” which stated:⁶

“A targeted drug whose clinical testing was led by Richard Stone, MD, of Dana-Farber Cancer Institute, has become the first new treatment for newly diagnosed acute myeloid leukemia (AML) in more than 25 years. . . The drug, midostaurin (Rydapt®), was approved by the U.S. Food and Drug Administration (FDA) as a combination treatment, with chemotherapy, for adult patients newly diagnosed with AML that carries a mutation in the gene FLT3. Such patients account for roughly a third of the 21,000 Americans

⁴ Manley PW, Caravatti G, Furet P, Roesel J, Tran P, Wagner T. Comparison of the profile of the AML drug midostaurin (Rydapt(R)) as a kinase inhibitor with those of its predominant primary human metabolites. *Blood*. 2017;130(suppl 1). Abstract 1383

⁵ Press Release. FDA approves new combination treatment for acute myeloid leukemia. FDA. April 28, 2017

⁶ Press Release. Backed by Dana-Farber research, FDA approves new AML drug. Dana-Farber Cancer Institute. April 28, 2017.

diagnosed annually with AML, a rare and aggressive disease of the blood and bone marrow.”

The Cost of Rydapt

According to Reuters, the list price at introduction was \$7,495 for 56 25mg capsules, or \$133.84 per capsule.⁷

An AML patient would typically receive 50mg twice a day (4 capsules), and the AMS patient would typically receive 100 mg twice a day (8 capsules).

The cost of the treatment depend upon the indication.

For AML, the cost would be \$535.36 per day and \$195,405.36 per year.

For an AMS patient, the cost is \$1070.71 per day and \$390,810.71 per year.

The Orange Book Patents for Rydapt

The March 19, 2018 version of the FDA Orange Book lists three patents for Rydapt. Two were assigned to Novartis AG (Basel, CH) and Dana-Farber Cancer Institute and one was assigned to solely to Novartis AG.

Table 1: The Orange Book patents for Rydapt

Patent number	Date filed	Date granted	Expiration	Inventors	Assignee
7973031	10/29/2002	7/5/2011	10/17/2024	Griffin; James D (Brookline, MA), Manley; Paul W (Arlesheim, CH)	Novartis AG (Basel, CH) Dana-Farber Cancer Institute Inc (Boston, MA)
8222244	5/17/2011	7/17/2012	10/29/2022	Griffin; James D (Brookline, MA), Manley; Paul W (Arlesheim, CH)	Novartis AG (Basel, CH) Dana-Farber Cancer Institute Inc. (Boston, MA)
8575146	6/17/2004	11/5/2013	12/2/2030	Coutre; Steven (Stanford, CA)	Novartis AG (Basel, CH)

⁷ Reuters Staff. [U.S. FDA approves Novartis' Leukemia Treatment](#). April 28, 2017.

The Griffin Patents that Failed to Disclose Federal Funding

The patents assigned to Novartis AG and the Dana-Farber Cancer Institute that failed to report NIH funding are listed in Table 2.

Table 2: The two FLT3 Griffin patents

Patent number	Priority date	Date filed	Date granted	Title
7973031	2001-10-30	10/29/2002	7/5/2011	Staurosporine derivatives as inhibitors of FLT3 receptor tyrosine kinase activity
8222244	2001-10-30	5/17/2011	7/17/2012	Staurosporine derivatives as inhibitors of FLT3 receptor tyrosine kinase activity

Note, the two patents have the exact same title and the same priority date of October 30, 2001. The first patent was filed in 2002, but not granted until 2011. The second patent was filed May 17, 2011.

On June 21, 2017, Novartis filed for an application for a patent term extension for patent 7,973,031, requesting an additional 1183 days.

On June 21, 2017, Novartis also requested a patent term extension for patent 8,222,244, for an additional 994 days.

The James Griffin Research Grants from the National Institutes of Health

NIH Grants for which James Griffin was a Principal Investigator

According to the National Institutes of Health RePORTER database, from 1985 to 2012 James Griffin was the principal investigator for grants involving 42 projects and 17 sub-projects awarded to the Dana-Farber Cancer Institute, with a total of \$32,655,809 in NIH funding.

Griffin received funding from the National Cancer Institute, the National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung and Blood Institute every fiscal year from 1985 to 2012.

From 2014 to 2017, James Griffin was the principal investigator for NIH grants to the Brigham and Women's Hospital involving 4 projects and 8 sub projects involving \$11,297,311.

A list of all 71 NIH projects and subprojects identifying James Griffin as principal investigator is attached as an Annex.

Of particular interest are the periods of funding from 1996 to 2001, leading up to the priority date for both patents, and from 2009 to 2011, leading up to the filing of the second patent.

Table 3: Funding by fiscal year for 71 NIH funded projects and subprojects listing James Griffin as the principal investigator, from 1985 to 2017

Year	Projects	Sub Projects	Total funding
1985	1		\$127,387
1986	1		\$116,972
1987	1		\$155,176
1988	2		\$267,469
1989	2		\$329,404
1990	2		\$382,739
1991	2		\$468,263
1992	2		\$485,919
1993	2		\$525,493
1994	2		\$512,094
1995	2		\$533,957
1996	3		\$2,534,049
1997	2	2	\$2,701,141
1998	2	4	\$3,232,873
1999	2	3	\$3,023,890
2000	2	2	\$2,755,613
2001	2	1	\$1,515,995
2002	1		\$298,972
2003	1		\$355,929
2004	1		\$355,929
2005	1		\$355,929
2006	1		\$347,565
2007	1		\$337,486
2008		1	\$302,258
2009	1	1	\$2,678,257

2010	1	1	\$2,724,533
2011	1	1	\$2,605,102
2012	1	1	\$2,625,415
2013			
2014	1	2	\$2,881,926
2015	1	2	\$2,806,128
2016	1	2	\$2,805,172
2017	1	2	\$2,804,085
Totals	46	25	\$43,953,120
Subtotal, 1996 to 2001	13	12	\$15,763,561
Subtotal, 2009 to 2011	3	3	\$8,007,892
Annual Average, 1996 to 2001			\$2,627,260
Annual Average, 2009 to 2011			\$2,669,297

Note that from 1996 to 2001, James Griffin was the principal investigator for grants averaging \$2.6 million per year, or \$7,198 per day, from the NIH, to study leukemia. This included, for example, six grants with the title “Novel Therapeutic Strategies in Leukemia and Lymphoma,” with a total grant amount of \$11,122,975.

Table 4: NIH grants from 1996 to 2001 with title: “Novel Therapeutic Strategies in Leukemia and Lymphoma.”

Project	Title	PI	Institution	Fiscal Year	NIH funding
1 P01 CA066996 01A1	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	1996	\$2,004,678

5 P01 CA066996 02	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	1997	\$1,990,293
5 P01 CA066996 03	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	1998	\$2,057,110
5 P01 CA066996 04	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	1999	\$2,035,202
5 P01 CA066996 05	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	2000	\$2,102,745
3 P01 CA066996 05S1	<u>Novel Therapeutic Strategies In Leukemia And Lymphoma</u>	Griffin, James Douglas	Dana-farber Cancer Institute	2001	\$932,947

These grants were cited in at least six papers published by James Griffin from 2002 to 2007, describing the elements of the patented inventions, including two papers that mention PCK412 (midostaurin) in the title of the paper.

Table 5: Seven papers published from 2002 to 2007 describing the role of FLT3 and PTK inhibitors for the treatment of leukemia cells.

Publication date	Citation	Authors	Disclosures
2002 June 1	(2002). <u>Inhibition of mutant FLT3 receptors in leukemia cells by the small molecule tyrosine kinase inhibitor PKC412</u> . Cancer Cell. 1 (5), 433-443.	Weisberg, E., Boulton, C., Kelly, L.M., Manley, P., Fabbro, D., Meyer, T., Gilliland, G., Griffin, J.D.	This work was supported in part by NIH PO1 CA66996 (D.G.G. and J.D.G.), a Leukemia and Lymphoma Society Specialized Center of Research Grant 7059 (D.G.G. and J.D.G.), and NIH PO1 DK50654 (D.G.G. and J.D.G.).
2002 Aug 13	(2002). <u>The roles of FLT3 in hematopoiesis and leukemia</u> . Blood. 100 (5), 1532-1542.	Gilliland, D.G., Griffin, J.D.	Supported in part by National Institutes of Health (NIH) PO1 CA66996 (D.G.G. and J.D.G.), a Leukemia and Lymphoma Society Specialized Center of Research Grant 7059 (D.G.G. and J.D.G.), and NIH PO1 DK5654 (D.G.G. and J.D.G.). D.G.G. is an Associate Investigator of

			the Howard Hughes Medical Institute.
2003 Feb 27	(2003). <u>Inhibition of FLT3 in MLL: Validation of a therapeutic target identified by gene expression based classification</u> . Cancer Cell. 3 (2), 173-183.	Armstrong, S.A., Kung, A.L., Mabon, M.E., Silverman, L.B., Stam, R.W., Den Boer, M.L., Pieters, R., Kersey, J.H., Sallan, S.E., Fletcher, J.A., Golub, T.R., Griffin, J.D., Korsmeyer, S.J.	This work was supported in part by NIH grants PO1 CA68484 and KO8 CA92551 and an American Society of Hematology Fellow Scholar Award (S.A.A.)
2004 Mar 2	(2004). <u>Combination of rapamycin and protein tyrosine kinase (PTK) inhibitors for the treatment of leukemias caused by oncogenic PTKs</u> . Proceedings of the National Academy of Sciences of the United States of America. 101 (9), 3130-3135.	Mohi, M.G., Boulton, C., Gu, T.L., Sternberg, D.W., Neuberg, D., Griffin, J.D., Gilliland, D.G., Neel, B.G.	This work was supported by National Institutes of Health Grants R01 DK50654 and PO1 DK50693 (to B.G.N.) and PO1 CA66996 (to J.D.G. and D.G.G.). D.G.G. is an Associate Investigator of the Howard Hughes Medical Institute. M.G.M. is supported by a fellowship from the Leukemia and Lymphoma Society.
2004 Sep 1	(2004) <u>Identifying and characterizing a novel activating mutation of the FLT3 tyrosine kinase in AML</u> . Blood. 104 (6), 1855-1858.	Jiang, J., Paez, J.G., Lee, J.C., Bo, R., Stone, R.M., DeAngelo, D.J., Galinsky, I., Wolpin, B.M., Jonasova, A., Herman, P., Fox, E.A., Boggon, T.J., Eck, M.J., Weisberg, E., Griffin, J.D., Gilliland, D.G., Meyerson, M., Sellers, W.R.	Supported by the Poduska Family Foundation, by the Claudia-Adams Barr Foundation (M.M. and W.R.S), by National Institutes of Health grant DK50654 and CA66996, and by the Leukemia and Lymphoma Society (D.G.G.). D.G.G. is an Associate Investigator of the Howard Hughes Medical Institute.
2004 Dec 20	(2005). <u>Patients with acute myeloid leukemia and an activating mutation in FLT3 respond to a small-molecule FLT3 tyrosine kinase inhibitor, PKC412</u> . Blood. 105 (1), 54-60.	Stone, R.M., DeAngelo, D.J., Klimek, V., Galinsky, I., Estey, E., Nimer, S.D., Grandin, W., Lebwohl, D., Wang, Y., Cohen, P., Fox, E.A., Neuberg, D., Clark, J., Gilliland, D.G., Griffin, J.D.	Supported in part by a Leukemia and Lymphoma Society SCOR grant (R.M.S., D.J.D., D.G.D., J.D.G.) and Leukemia and Lymphoma Society grants (V.K. and S.D.N.) and by National Institutes of Health grant PO1 CA66996-06.
2007 Jul 9	(2007). <u>Potentiation of antileukemic therapies by Smac mimetic, LBW242: effects on mutant FLT3-expressing cells</u> . Molecular Cancer Therapy. 6 (7), 1951-1961.	Weisberg, E., Kung, A.L., Wright, R.D., Moreno, D., Catley, L., Ray, A., Zawel, L., Tran, M., Cools, J., Gilliland, G., Mitsiades, C., McMillin, D.W., Jiang, J., Hall-Meyers, E., Griffin, J.D.	J.D. Griffin is supported by NIH grant CA66996 and a Specialized Center of Research Award from the Leukemia and Lymphoma Society. J.D. Griffin is also supported by NIH grants CA36167 and DK50654. L. Zawel and M. Tran are employees of Novartis Pharma AG, Basel, Switzerland. J.D. Griffin has a financial interest with Novartis Pharma AG.

Note that Griffin also cited support from NIH grants CA36167 and DK50654.

There were at least 24 projects funded under grant CA306167 where Griffin was the principal investigator from 1985 to 2007, of which 23 are included in the NIH RePORTer database. We are attaching the titles and links to the 23 CA306167 grants as an Annex.

There were seven DK50654 grants, and these are listed in Table 6.

Table 6: Seven DK050654 projects listing James Griffin as the PI and Dana-Farber as the institution.

Project	Project Title	FY	Funding IC	Total cost
1 P01 DK050654 01A1	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	1996	NIDDK	Unavailable
1 P01 DK050654 02	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	1997	NIDDK	\$210,597
3 P01 DK050654 03S1	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	1998	NIDDK	\$198,808
5 P01 DK050654 03	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	1998	NIDDK	\$198,808
5 P01 DK050654 04	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	1999	NIDDK	\$198,808
5 P01 DK050654 05	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	2000	NIDDK	\$148,636
3 P01 DK050654 05S1	Signal Transduction Pathways In Stable Phase Chronic Myeloid Leukemia Cells	2001	NIDDK	\$296,752

There are several other grants that appear to be related to the inventions in the Rydapt patents, including the second patent, 8,222,244, which was filed on May 17, 2011.

For example, the CA066996 projects listed in Table 7, totalling \$8.3 million and averaging more than \$2 million per year, are particularly relevant. Several elements of the grant abstracts are directly related to the claims for patent 8,222,244.

Table 7: CA066996 grants from 2008 to 2011

Project	Title	Fiscal Year	Cost
P01 CA066996 11A1	Tyrosine Kinase Oncogenes In Acute Myeloid Leukemias	2008	\$302,258
P01 CA066996 12	Tyrosine Kinase Oncogenes In Acute Myeloid Leukemias	2009	\$311,047
P01 CA066996 12	Development Of Novel Therapeutic Strategies In Human Leukemias	2009	\$2,367,210

P01 CA066996 13	<u>Tyrosine Kinase Oncogenes In Acute Myeloid Leukemias</u>	2010	\$315,567
P01 CA066996 13	<u>Development Of Novel Therapeutic Strategies In Human Leukemias</u>	2010	\$2,408,966
P01 CA066996 14	<u>Tyrosine Kinase Oncogenes In Acute Myeloid Leukemias</u>	2011	\$298,834
P01 CA066996 14	<u>Development Of Novel Therapeutic Strategies In Human Leukemias</u>	2011	\$2,306,268

James Griffin's research directly related to the patented invention was robustly supported by the NIH during the years preceding the dates for the priority and the filing of both patents.

Requested Remedies for Non-disclosure

The Bayh-Dole Act and federal regulations and guidelines obligate contractors to disclose government rights in subject inventions, including via: (1) a requirement to disclose within a reasonable time that federal funding contributed to a subject invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

After establishing a failure by the patent holder to disclose the federal funding, an agency may choose to require the patent holders to provide a disclosure to iEdison and to submit a Certificate of Correction to the United States Patent and Trademark (USPTO). The agency also has consequential remedies. In particular, a failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the federal government to "receive title to any subject invention not disclosed to it within such time."

The disclosure itself is an acknowledgement that the federal government has certain rights in the patents, and that the patent holder has certain obligations. When federal funding is involved, the patent owner has an obligation to manufacture the invention substantially within the United States and to make the invention "available to the public on reasonable terms." The federal government obtains a worldwide royalty-free right to use the patent, and may grant a compulsory license to the patent under the Bayh-Dole march-in provisions of 35 U.S.C. § 203(a).

The failure to make a timely disclosure of the federal funding should be seen as an attempt to evade these responsibilities and as a denial of the government's rights in the invention.

KEI recommends that the federal government take title to the invention, since the lesser remedy of requiring late disclosure has not, in the past, provided an adequate incentive for patent holders to comply with the disclosure obligations.

See the Annex attached as a PDF file and also published as [KEI Briefing Note 2018:1](#), regarding the discussion of the specific statutory, regulatory and contractual obligations to disclose federal funding in patented inventions, and the remedies when funding is not disclosed.

Attachments:

ANNEX: James Griffin's 71 NIH Funded Projects
ANNEX: Griffin's CA36167 Grants, from NIH REPORTER
ANNEX: KEI-Briefing-Note-2018-1



March 21, 2018

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
Email: hammerslaa@od.nih.gov

Dear Director Hammersla:

I am enclosing a memorandum and five attachments that describe two patents granted to James Griffin and assigned to the Dana-Farber Cancer Institute each with the same title:

Staurosporine derivatives as inhibitors of FLT3 receptor tyrosine kinase activity

Patents 7,973,031 and 8,222,244 are listed in the FDA Orange Book for the drug Rydapt (INN midostaurin), which is an expensive drug for the treatment of leukemia, including specifically acute myeloid leukemia (AML), myelodysplastic syndrome and advanced systemic mastocytosis (ASM).

The cost of Rydapt depends upon the indication and patient weight. For a typical patient, the cost for the treatment of AML is \$195,405 per year, and for ASM, \$390,811 per year. In both cases, the high cost is a barrier to access and a fiscal strain on health systems.

We believe both patents were based upon research funded by the NIH. Neither of the patents disclose federal funding.

Griffin has been working in the field of leukemia research since 1985 and has received over \$44 million in funding for 71 projects (and subprojects) where he was the principal investigator. Many of these NIH grants were during the time period of and on topics related to the patents at issue, including over \$15 million in grants between 1996-2001, leading up to the priority date of both patents, and over \$8 million in grants between 2009-2011, leading up to the filing date of the second patent. Griffin was the co-author of papers that describe the invention, refer specifically to midostaurin, and disclose NIH funding.

The memorandum asks the NIH to take title to the patents as a remedy for the failure by Griffin to acknowledge the NIH funding in the patent application, as required by law.

Sincerely,



Andrew S. Goldman, Esq.
Counsel, Policy and Legal Affairs
andrew.goldman@keionline.org



James Love, Director, KEI
james.love@keionline.org
+1.202.332.2670

Attachments:

MEMORANDUM: Rydapt (INN midostaurin): Failures to disclose government funding for patents granted to James Griffin and assigned to Dana-Farber Cancer Institute in the FDA Orange Book, KEI Series on inventors that fail to disclose U.S. government funding in patented inventions, March 21, 2018

ANNEX: James Griffin's 71 NIH Funded Projects
ANNEX: Griffin's CA36167 Grants, from NIH REPORTER
ANNEX: KEI-Briefing-Note-2018-1

Cc: The Honorable Daniel R. Levinson, Dan.Levinson@oig.hhs.gov

From: Kirby, Tara (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=2368A591FA4C4932A802E5D467FB49ED-TARAK]
Sent: 3/13/2019 5:08:43 PM
To: ELCG Short [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ff6e4c0e2cd94f9d9584209855fd9fa1-ELCG]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Shmilovich, Michael (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7dfe19bfd1d443ceb700b9f22d159a90-shmilovm]
Subject: Final/Preliminary Determination Bypass Request
Attachments: A-058-2019_Final_Determination.docx; 2019_02_20_License_Application [b4] pdf; A-233-2019_LetterResponse to [b4] Objection_3-12-19.docx; ELCG - 062618.docx

Good afternoon folks,

We have received a bypass request from Jaime Greene (via Richard Rodriguez) at NCI-TTC, concerning a combined Preliminary/Final Determination. If you review the procedure document for ELCG bypass (the last attachment), you will see that the process does not currently contemplate bypasses for anything other than Preliminary Determinations; however, I have agreed to present this matter to the ELCG Representatives for review.

In this instance, I have two requests for the group:

- (1) Please review the Determination and accompanying documentation, and by **1 pm on Friday, March 15** provide feedback to Jaime and Richard on any issues or concerns, and whether you believe a formal presentation to the ELCG is necessary; please also copy Misha and myself.
- (2) Please email me separately to provide your opinion [b5]

b5

Thanks,
Tara

Tara L. Kirby, Ph.D.
phone: +1-240-669-5128
email: tara.kirby@nih.gov

Disclaimer: The information in this email and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the originally intended recipient. If you have received this email in error, please inform the sender and delete it from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases shall not accept liability for any statements made that are the sender's own and not expressly made on behalf of NIAID by one of its representatives.

From: Rodriguez, Richard (NIH/NCI) [E]
Sent: Tuesday, March 12, 2019 3:45 PM
To: Kirby, Tara (NIH/NIAID) [E] <tara.kirby@nih.gov>
Subject: Jaime's Final/Preliminary Determination Bypass Request

Hi Tara,

REL0000024470

Please find attached the docs for Jaime's requested ELCG bypass. She is out of the office, so I will try and answer any questions that come up.

Thanks,

Richard

RICHARD U. RODRIGUEZ

Associate Director

Patent Agent

Technology Transfer Center

National Cancer Institute

9609 Medical Center Drive, Rm 1E530

Bethesda, MD 20892-9702 (USPS)

Rockville, MD 20850-9702 (UPS:FedEx/Visitors)

Phone: 240-276-6661

Fax 240-276-5504

<https://techtransfer.cancer.gov>

"Engaged partnerships benefiting research, innovation and public health."

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DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Cancer Institute
Technology Transfer Center
9609 Medical Center Drive
Rockville, MD 20892

DATE: March 12, 2019

TO: Richard U. Rodriguez, M.B.A.
Associate Director, TTC, NCI

THROUGH: David Lambertson, Ph.D.
Sr. Technology Transfer Manager, TTC, NCI

FROM: Jaime M. Greene, M.S.
Sr. Technology Transfer Manager, NCI, TTC

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SIGNATURE

Richard U. Rodriguez, MBA
Associate Director
Technology Transfer Center
National Cancer Institute

Attachments:

b4 License Application
Letter

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New Procedure for ELCG Review of Non-Complex PDs

Representatives from the intramural Technology Transfer Community (TTC), the NIH Office of Technology Transfer, and the Director, NIH Office of Intramural Research met to evaluate how the Exclusive License Consultation Group (ELCG) has functioned over the past year or so and if any modifications need to be made to how the ELCG functions. In addition, various members of the group raised concerns that the participants acknowledged, discussed thoughtfully, and agreed on a path moving forward.

Meeting Participants

Michael Gottesman (Organizer)
Mark Rohrbach (OD/OSP/TTIP)
Karen Rogers (OD/OIR/OTT)
Claire Driscoll (NHGRI)
David Bradley (NIDCR)
Charles Niebyski (NIDDK)

Richard Rodriguez (NCI)
Lili Portilla (NCATS)
Charles Salahuddin (NIMH)
Alan Deutch (NHLBI)
Michael Mowatt (NIAID)

Also discussed was whether or not a change should be made to the current requirement that all IC Technology Transfer Offices (TTOs) present all Preliminary Determinations (PDs) and Federal Register (FR) notice objections for exclusive license to the ELCG before publishing notices in the FR and/or executing exclusive licenses. It was agreed that the ELCG, while only serving a consulting role, still provides valuable review and helpful advice. Maintaining the group ensures transparency, consistency and continuity in licensing practices across all TTOs now that the community operates in a decentralized manner. It was also agreed that the ELCG is a good forum for exchanging best practices and insights into more complex licensing activities.

With respect to presenting PDs to ELCG, two concerns were raised: 1) requiring review by the ELCG for every PD sometimes leads to delays in executing licenses; and 2) ELCG review of non-complex PDs is not necessary in most cases. It was agreed that from now on IC TTOs would identify non-complex PDs and could choose to bypass the ELCG for any such PDs. In these instances, the IC would be required to provide 48 hours (two business days) notice (by email) to the ELCG members of their IC's decision to proceed with the publication in the FR of the intent to grant an exclusive license. The draft PD and/or FR notice would be sent to the ELCG chair, who would then forward the document(s) or otherwise convey their location to the appointed ELCG representatives from the ICs, OTT and to the Special Advisor for Technology Transfer, representing the Deputy Director, for Intramural Research. The intent of the 48 hour-notice is to provide an opportunity for ELCG members to alert the IC before publication to any substantive issues or concerns regarding the PD and/or FR that would necessitate a formal presentation to the ELCG at one of their biweekly in-person meetings. No response within 48 hours from this group confirms that the IC is free to move forward.

It was also agreed that the community would revisit this new guidance in 6 months to determine if any changes need to be made to this guidance.

With respect to presenting FR notice objections to ELCG, it was agreed that current procedures will remain in place.

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 9/25/2018 1:25:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: James Douglas Griffin; CA066996

Mark:

b4,b5

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, September 24, 2018 3:13 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 24, 2018 3:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

b4,b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 24, 2018 3:02 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: James Douglas Griffin; CA066996

Try this instead:

b4,b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 24, 2018 3:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: James Douglas Griffin; CA066996

b4,b5

From: Merritt, William (NIH/NCI) [E]
Sent: Thursday, September 20, 2018 2:53 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Hi Ann,

b4,b5

Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 17, 2018 10:15 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: James Douglas Griffin; CA066996

Good Morning: I just sent an outlook invite for 2:00 this Thursday, September 20th. I will link both of you. Just send me your telephone number.

Thanks for your assistance.

Ann

REL0000024472

From: Merritt, William (NIH/NCI) [E]
Sent: Monday, September 17, 2018 9:48 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Yes, I am free at various times on Thursday; unsure about about AM right now, awaiting an agenda; but around 2 is good, also 4?

Bill

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, September 17, 2018 8:07 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: James Douglas Griffin; CA066996

Good Morning Bill: Would Thursday 9/20 be better for you? I am open most of the day. Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Thursday, September 13, 2018 4:10 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

I have a full afternoon on Tuesday with meetings until 6, and Wednesday afternoon I am booked until 4, but would be available at that time (4 – 6 time frame) for this call.

b4,b5

b4,b5

Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Thursday, September 13, 2018 3:53 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: James Douglas Griffin; CA066996

Hello Bill:

We are at the final stages of NIH's review of the NIH funded grants and the inventions for Rydapt.

b4,b5

b4,b5

It would be helpful if you, Mark Rohrbaugh (who assists in similar requests from OSP) and you discuss the NCI grants and the results with the testing of the compounds.

Are you available next week? Would Tuesday, September 18 after 3 or Wednesday after 1 be convenient? If not can you suggest another time. The discussion is intended to identify the distinctions, if any, between NIH funding, and the actual results of the testing of the named compounds.

Thank you again for your assistance.

Ann

From: Merritt, William (NIH/NCI) [E]

Sent: Wednesday, July 11, 2018 11:50 AM

To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

Subject: RE: James Douglas Griffin; CA066996

Ann - I checked the P01 again,

b4,b5

b4,b5

Bill

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, July 11, 2018 10:59 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Morning Bill:

I have a follow-up question for you:

b4,b5

Thank you again for your assistance.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, July 09, 2018 6:08 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Good Morning Bill:

Thank you for your detailed analysis. I will keep you updated on the next steps.

REL0000024472

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Friday, July 06, 2018 7:58 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann –

I'm very sorry for the delay in responding, but finally now today I have had a (first) chance to get to this and other long delayed work, since some regular meetings were canceled.

b4,b5

Regards,
Bill Merritt

William D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, June 25, 2018 10:57 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Bill:

Do you have any questions regarding your review of CA066996?

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Monday, May 21, 2018 3:06 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

REL0000024472

Ann,

Thanks for this instructive drill down for explanation of these terms, important in my review of this issue.

Will be in touch,
Bill

William D. Merritt, Ph.D.

Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, May 21, 2018 2:36 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Dear Bill:

Thank you for taking your time today to discuss CA066996 and if the supported research was used for the conception or reduction of Rydapt.

The definition of "subject invention" that is defined by the Bayh-Dole statute and regulation is: "any invention of the contractor conceived for first actually reduced to practice in the performance of work under this contract...."

"Conception" and "first actually reduced to practice" is not defined in the Bayh-Dole statute. The following are definitions taken from the patent examiner's procedure manual or a law firm specializing in patent law.

"Conception" is defined in the patent examiner's procedures as "the complete performance of the mental part of the inventive act" and it is "the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is thereafter to be applied in practice...."

Another definition of "Conception" from a law firm:

Conception is the touchstone of inventorship, the completion of the mental part of invention. It is "the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation.

The patent examiner's procedures defined "reduction to practice" as

Reduction to practice may be an actual **reduction** or a constructive **reduction to practice** which occurs when a patent application on the claimed invention is filed. The filing of a patent application serves as conception and constructive **reduction to practice** of the subject matter described in the application.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 3:23 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Dear Bill:

I have attached the KEI request for NIH to take title or other actions to the patents in question. I have also attached Dana Farber's response and 3 citations to publications (2 have abstracts) that link Dr. Griffin's funding on two publications to CA066996. I have also identified over 100 other publications that are being reviewed.

I will send you an outlook meeting time for Monday. Thank you again for your assistance.

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Tuesday, May 15, 2018 11:33 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

I am leaving town very soon to attend a conference the rest of the week. So next Monday morning would be the first opportunity to talk. It may be helpful to send the information as background to me so I can look it over before we speak.

Best regards,
Bill Merritt

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 11:17 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: James Douglas Griffin; CA066996

Dear Dr. Merritt:

NIH received a request from Knowledge Ecology International (KEI) requesting NIH to take multiple actions, including, taking title to certain patents filed by the Dana Farber Institute for inventions made by Dr. James Douglas Griffin that have led to the therapeutic Rydapt®. According to QVR you are listed as the PO for the above grant that Dr. Griffin is supported on. In order to respond to the KEI request an understanding and information is needed to determine if there is a link between Dr. Griffin's NIH funding and the development of this therapeutic. Rydapt® is used for the treatment of acute myeloid leukemia, myelodysplastic syndrome and advanced systemic mastocytosis. There are 2 patents that Dr. Griffin is identified as an inventor that the FDA reports are used in the commercialization of Rydapt®. Both of the patents' abstracts state:

The present invention relates to the use of staurosporines derivatives for the preparation of a drug for the treatment of diseases involving deregulated FLT3 receptor tyrosine kinase activity, especially for the curative

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and/or prophylactic treatment of leukemias and myelodysplastic syndromes, and to a method of treating diseases involving deregulated FLT3 receptor tyrosine kinase activity.

Before sending you additional background information you may need to identify the issues that have been raised, it may be helpful if we talked first. Or, if you prefer I can forward you the information received by KEI and the summaries prepared thus far for your review.

Please let me know when you are available for a 30 minute discussion. If it helps I am available this Thursday or Friday afternoon and Monday May 21 in the morning. Let me know if you would like to receive the background information before we talk.

Thank you in advance for your assistance.

Ann

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Li, Chanel (NIH/OD) [C] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D4BEEA214A074DCF8820DC28D0B70655-LIC17]
Sent: 4/20/2018 3:45:28 PM
To: O'Reilly, Marina (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=54d6c68e99e94ea6bc7872cfbf0d0176-oreillym]; Jambou, Robert (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ff42a9fa39824980aa9e36af49e56cbc-jambour]; Rosenthal, Eugene (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=516242ed831440f0b1481136b0899621-rosenthe]; Singh, Aparna (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=219f4d69379c4ba6987034c243b10c5d-singhap]; Montgomery, Maureen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7e66e537ddd9415ea41e2644209f69a8-montgom]; Tucker, Jessica (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2baf4ae78d90412dbefbfb5e52c31a4-tuckerjm]; Gadbois, Ellen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0243d1d6e6f248268d2edec566c26c2a-gadboisel]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: NIH is sued for plans to award exclusive license for CAR-T therapy to Gilead

A patient advocacy group has filed a lawsuit to block the federal government from awarding an exclusive license to Gilead Sciences (GILD) for an experimental cancer therapy, arguing that the potential for a high price may preclude access to many Americans.

At issue is a CAR-T treatment, which relies on the immune system to attack cancer cells. Last December, the National Institutes of Health indicated plans to award a worldwide exclusive license to a CAR-T treatment that is being developed with taxpayer funds to Kite Pharma, which had recently been purchased by Gilead.

The advocacy group, Knowledge Ecology International, contended in its lawsuit filed on Thursday that the federal government should not award a license to Gilead without securing an agreement that any emerging medicine is affordable to Americans. The group also believes the NIH should not consider licenses until development work is done in order to assess the effectiveness of the medicine and wield greater leverage in any negotiation.

https://www.statnews.com/pharmalot/2018/04/20/nih-sued-license-gilead-car-t/?utm_campaign=rss

From: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=JORGENSENLA]
Sent: 6/30/2017 3:46:14 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: RE: WSJ article/interview--urgent

Mark and Ann -

Please note that I told them I pulled the language from the response 100% - I did no drafting! It is basically the opening and closing. I did not think [b5]
[b5]

-----Original Message-----

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Friday, June 30, 2017 11:01 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>; Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Bayha, Ryan (NIH/OD) [E] <bayhar@od.nih.gov>; Burklow, John (NIH/OD) [E] <BurklowJ@OD.NIH.GOV>; Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Subject: FW: WSJ article/interview--urgent

Hi Mark and Ann-

For your awareness, Carrie received an inquiry from the Wall Street Journal asking for her to comment on whether OSP is going to look at licensing related to CRISPR, please see the email from the reporter below. We will respond with the statement below attributable to the Office of Science Policy. Lyric drafted the statement with language from the recent OER/OSP KEI response.

Statement:

Among the benefits derived from NIH-conducted and supported biomedical research are effective and broadly accessible new healthcare treatments and services that benefit the public. Practical realization of these benefits depends on the ability and willingness of private sector partners to develop and commercialize new technologies arising from NIH-funded research. When NIH funding leads to a patented invention, NIH policies provide guidance to institutions licensing the patents to facilitate on-going scientific research with the patented technology and, at the same time, provide appropriate incentives for commercial development.

The relevant NIH policies are stated in Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, December 23, 1999: https://grants.nih.gov/grants/intell-property_64FR72090.pdf

While we have not received any inquiries or complaints about lack of access to the CRISPR-CAS9 technology for research or commercial development from those who are in a position to use the technology, we continue to monitor access and use of the CRISPR technology that was funded by NIH with respect to public access and compliance with NIH principles and policies. At this time, we do not believe that a new NIH policy to address the licensing of CRISPR patented technology is necessary.

Thank you-
Emma

----- Original message -----

From: "Marcus, Amy" <amy.marcus@wsj.com<mailto:amy.marcus@wsj.com>>
Date: 6/29/17 9:47 PM (GMT+01:00)
To: "Wolinetz, Carrie (NIH/OD) [E]" <carrie.wolinetz@nih.gov<mailto:carrie.wolinetz@nih.gov>>
Subject: WSJ article/interview--urgent

Dear Carrie,

We've spoken about Crispr before, and I wanted to reach out to you about a story I'm working on with a colleague at the WSJ about growing interest by a number of researchers, academics, and others in getting NIH to take a closer look at Crispr licensing policies. They are arguing that the exclusive licenses given to the Crispr-related spin-outs from Broad and Berkeley cover human disease too widely and may therefore create a chilling effect on other companies interested in an opportunity to develop therapies. We understood that some groups and individuals have requested that OSP review the issue, since NIH funding supported Crispr research.

We are working on a very tight deadline on this story and I wanted to get your thoughts and comments for the piece. Is OSP going to take a look at licensing related to Crispr--and/or consider doing so? Are you available for a call to discuss further today/tomorrow/Monday? Thanks and best,

REL0000024475

Amy

Amy Dockser Marcus

Staff ~~Reporter~~ The Wall Street Journal

C: [REDACTED] **b6**

From: Kassilke, Deborah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=KASSILKE]
Sent: 1/19/2017 10:05:23 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: DRAFT RESPONSE to KEI
Attachments: KEI LOVE Qs 011217.docx

Mark – as discussed please take a read through? Thanks I’m again attaching the 3 requests they sent to our office if you want to reference.

Mr. Love –

b5

Deborah Kassilke
Director, Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852
E-Mail: Deborah.Kassilke@nih.gov
Phone: 301-435-5294
Cell: b6

From: Joe Allen [jallen@allen-assoc.com]
Sent: 5/15/2019 9:55:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Re: Jamie Love's response to Fred Reinhart and NIH CRADAS

Agreed. I'd heard somewhere that the updated paper Ashley and you have pending includes some data on the relative contributions government and industry made in the development of several of the commercialized drugs arising from NIH supported research. True?

I just suggested to Steve Susalka that now that we have Jamie Love out in the open, a point by point rebuttal of his "facts" could be very powerful, assuming we can compile the data. For example, from my recollection Sen. Bayh's letter on Cell Pro was arguing that the Johns Hopkins licensee wasn't developing the drug, not that it wasn't "reasonably priced."

Thoughts?

On 5/15/2019 5:49 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> The MCRADA is just a streamlined version of a standard CRADA when the primary exchange from the company is materials and much less scientific collaboration. NIH had done these all the time but simplified the process of negotiation by taking out the clauses that would not apply to this sort of "collaboration". In this sense it is not a new category but just a better way of doing business and shortened negotiation time. They all are counted as CRADAs and have the same legally required terms such as giving the outside party an exclusive option to apply for an exclusive license to any invention made under the CRADA.

> There was a drop later when Dr. Zerhouni announced that NIH scientists could no longer engage in private sector consulting ON THEIR OWN TIME. It took at least a year of my effort and that of my colleagues to educate scientist and companies that there was no restraint of official duty collaborations such as CRADAs.

> The fact that NIH affirmed that the increase in CRADA collaborations was due to the removal of the reasonable pricing clause, long before the issue of drug pricing because so dominant, suggests that it is real.

> -----Original Message-----
> From: Joe Allen <jallen@allen-assoc.com>
> Sent: Wednesday, May 15, 2019 5:05 PM
> To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
> Subject: Jamie Love's response to Fred Reinhart and NIH CRADAS

> His response to Fred's earlier column just went up:
> <https://www.ipwatchdog.com/2019/05/15/jamie-love-responds-criticism-knowledge-ecology-international-letter/id=109239/>

> Note his critique of the decline in NIH CRADAS per the reasonable pricing clause as well as his claims on government investment in several drugs. Worth mulling over how to respond.

>
--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(C) b6
www.allen-assoc.com

REL0000024480

From: Ano, Susan (NIH/NINDS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=4D6832E1B254404783859CF30CB352D2-ANOS]
Sent: 10/6/2017 5:41:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

FYI, based on a quick review of the technology, b5

Best regards,

Sue

Susan Ano, Ph.D.
Technology Development Coordinator
Office of Technology Transfer
The National Institute of Neurological Disorders and Stroke
The National Institutes of Health
Mail address: 31 Center Drive, Suite 8A52, MS2540
Bethesda, MD 20892 USA
Physical location: 35 Convent Drive, Room GF146
Bethesda, MD 20892 USA
phone (301) 435-5515
cell b6



National Institute of
Neurological Disorders
and Stroke

Have patience. All things are difficult before they become easy."

— Saadi, poet

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, October 06, 2017 10:17 AM
To: NIH TDC Short <niaaatdcs-l@mail.nih.gov>
Subject: FW: KEI asks HHS to use B-D right in Zinbryta patent (multiple sclerosis)

NOTE this product utilizes NIH licensed patents based in inventions made by NINDS and NCI scientists. The formal "March-In" proceedings of Bayh-Dole do not apply to intramural inventions. However, article 5.4b of the model exclusive license reads:

"In exceptional circumstances, and in the event that the Licensed Patent Rights are Subject Inventions made under a CRADA, the Government, pursuant to 15 U.S.C. §3710a(b)(1)(B), retains the right to require the Licensee to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the Licensed Patent Rights in the Licensed Field of Use on terms that are reasonable under the circumstances, or if the Licensee fails to grant this license, the Government retains the right to grant the license itself. The exercise of these rights by the Government shall only be in exceptional circumstances and only if the Government determines:

(i) the action is necessary to meet health or safety needs that are not reasonably satisfied by the Licensee;

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- (ii) the action is necessary to meet requirements for public use specified by Federal regulations, and these requirements are not reasonably satisfied by the Licensee; or
- (iii) the Licensee has failed to comply with an agreement containing provisions described in 15 U.S.C. §3710a(c)(4)(B);

-Mark

<http://www.keionline.org/node/2867>

KEI asks HHS to use Bayh-Dole rights in Zinbryta patent (drug for multiple sclerosis)

Submitted by KEI Staff on 14. September 2017 - 12:30

- [Medical Technologies](#)

Attached is a letter sent on September 14, 2017 to Andrew Bremberg, an Assistant to the President and the Director of the Domestic Policy Council at the White House, and Keagan Lenihan, a Senior Adviser to HHS Secretary Tom Price, regarding Zinbrytra (INN: daclizumab), a drug to approved by the FDA to treat multiple sclerosis. (PDF version [here](#))

This is an older drug, and the NIH obtained a patent on its use to treat multiple sclerosis, and licensed the patent on a exclusive basis to Biogen. Biogen and Abbvie market the drug around the world. The price in the United States is more than \$96,000 per year (\$7390 per injection every 4 weeks, 13 times a year), but far lower in every high income country where KEI obtained prices.

The letter asks DHHS to use one or more of three federal rights in the NIH licensed patent to "authorize affordable competition, or to force Biogen to lower its price." The three actions include using the royalty free right in the patent, exercising march-in rights, or terminating the license. The option to terminate the license is featured in the letter, and it is an action that KEI had not focused on previously.

The termination clause is something the U.S. government can do with government owned patents, including any owned by the NIH.

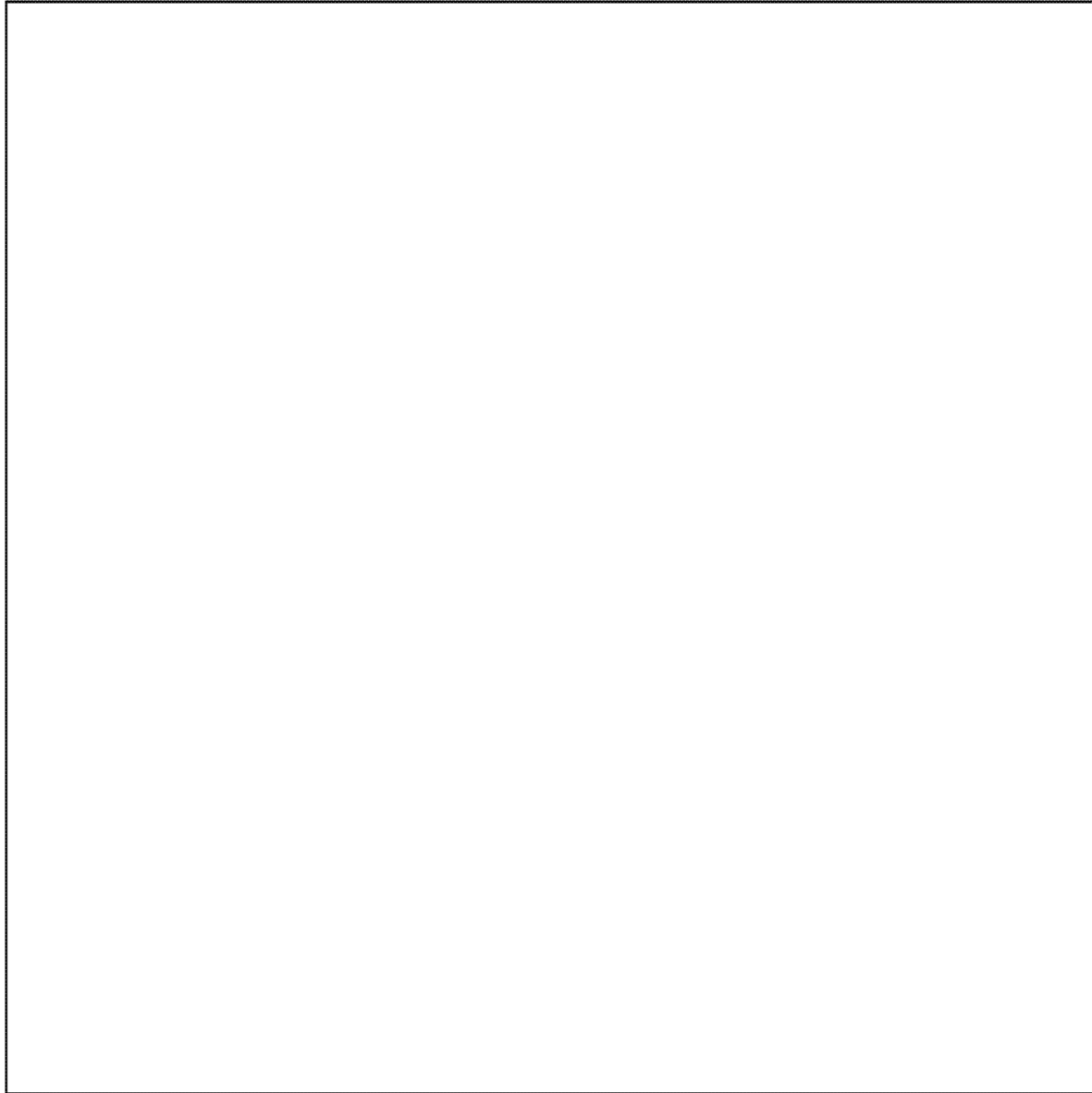
At the end of this blog is a graph of the prices of MS drugs, over time.

Below is an excerpt from the beginning and another excerpt from the end of the letter.

We write to you today with regard to the excessive price of an important drug for multiple sclerosis called daclizumab, co-marketed by Biogen and AbbVie as Zinbryta at prices roughly 3 to 4 times higher in the United States than in other high income countries. The patent for Zinbryta was licensed from the NIH, and under the Bayh-Dole Act there are three specific actions the United States government can and should utilize to authorize affordable competition, or to force Biogen to lower its price. These include: (1) making use of the government's royalty-free rights in the patent; (2) utilizing the "march-in" right to license the patent to a third party; and/or (3) terminating the exclusive license.

Amidst a crisis of out-of-control drug prices, this is an instance where the federal government has the power to act without the need for any additional statutory authority.

[snip]



[snip]

The United States prices are 2.8 to 4.3 times higher than any of the reference countries. The U.S. price is 2.8 times higher than Norway and Denmark and 3.8 times higher than Switzerland, even though all three of these countries have higher per capita incomes than the United States, and the U.S. taxpayers funded the relevant discovery and own the patent.

There is no reason to accept a foreign price, even from a country of a similar per capita income, as reasonable. But in our opinion, it is unreasonable for Biogen/Abbvie to charge higher prices in

the United States than in other large economies with a per capita income at least 50 percent of the United States.

In this case, prices in the U.S. are not only higher — they are 180 to 330 percent higher than every high income country where KEI could obtain pricing data. The pricing of Zinbryta is contrary to statutory requirement of the Bayh-Dole Act to make the inventions available to the public on reasonable terms.

A failure by HHS to address the discrimination against U.S. residents in pricing harms everyone who buys or reimburses the drugs, including all U.S. taxpayers, all employers who pay for health benefits, and many persons living with multiple sclerosis who face daunting co-payments, who are underinsured, or who never get the drug because of its high cost.

Conclusion

We request that the Department of Health and Human Services use one or more of the three options at its disposal under the Bayh Dole Act to lower prices of this important MS drug, including:

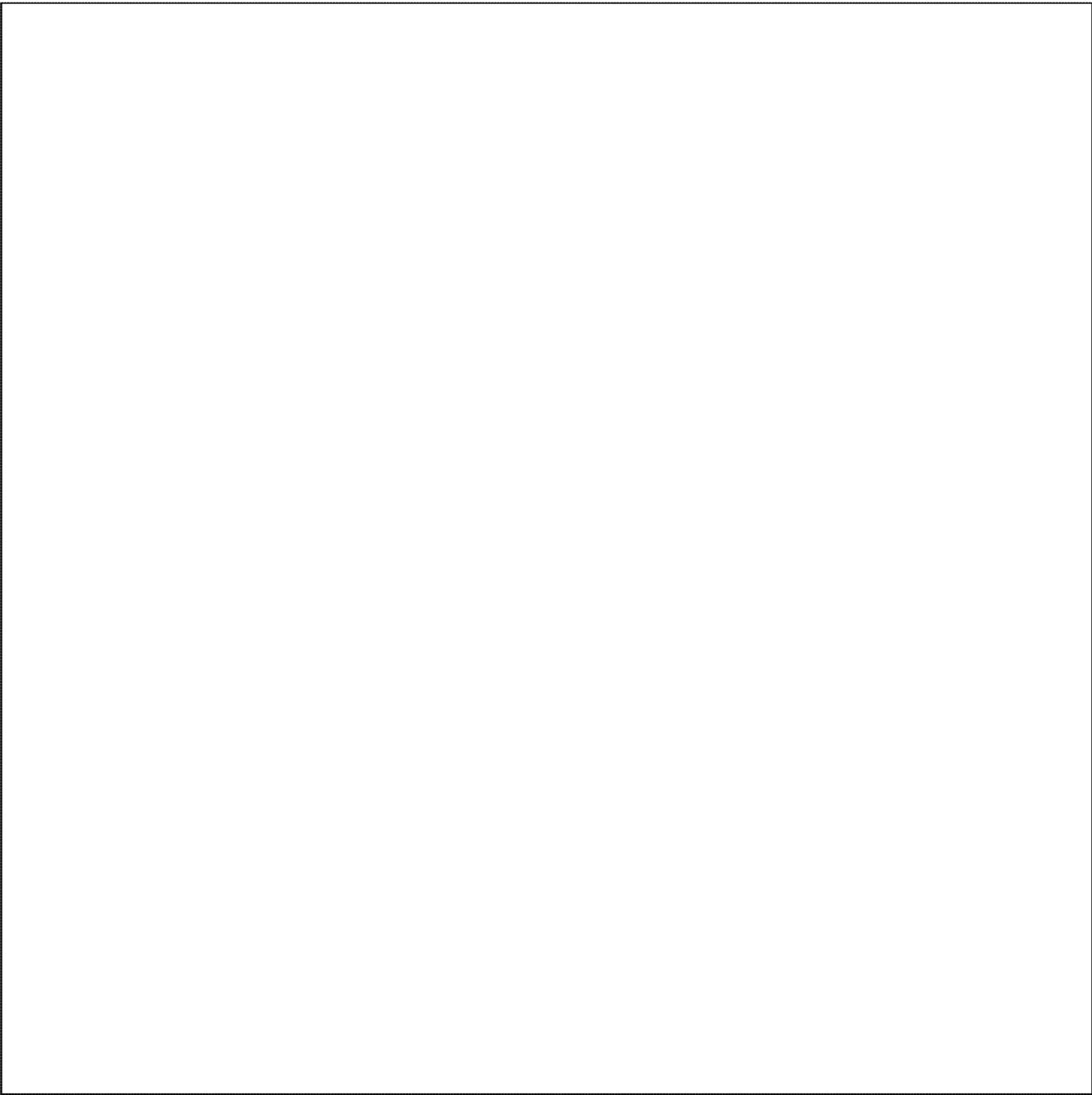
- (1) under 35 U.S.C. § 209(d)(1), utilizing the royalty-free license in the government-owned patent to authorize generic competition;
- (2) under 35 U.S.C. § 203(a), utilizing the “march-in” rights to license the drug to a third party; or
- (3) 35 U.S.C. § 209(d)(3), terminating the exclusive NIH license to Abbott/Biogen on the ground that the company is failing to abide by its obligation to make to invention “available to the public on reasonable terms”.

Specifically, this letter should be seen as request to exercise march-in rights under 35 U.S.C. § 203(a), and/or to terminate the license under 35 U.S.C. § 209(d)(3), on the grounds that charging U.S. residents 2.8 to 4.3 times more than residents in other high income countries is on its face unreasonable, and in violation of the requirement in 35 U.S.C. § 201(f) to make the invention covered by the license “available to the public on reasonable terms.” We also urge DHHS to use the royalty-free right in the patents to exercise leverage and freedom to operate whenever it faces challenges in implementing its section 203 or 209 rights.

We believe that terminating the exclusive license may be the best option, because it will provide the most leverage and the most flexibility in terms of obtaining alternative supplies of the product. But a credible threat to use any of these three options will be sufficient to force Biogen and AbbVie to lower its price of Zinbryta, at least to the prices that the companies already charge in other countries with incomes similar to the United States.

The Trump Administration has made numerous public pronouncements regarding the need to fight high drug prices, a policy point supported by overwhelming public opinion. In this instance, the government has all of the leverage it needs to take strong, decisive action to benefit multiple sclerosis patients, consumers, and taxpayers.

We request a meeting at your earliest convenience to discuss this matter further.



From: Soukas, Peter (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=B1F6020157AC47948C6E34166B78E433-SOUKASP]
Sent: 1/10/2019 10:23:21 PM
To: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Puglielli, Maryann (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9f53ceacaf754875a948081bac5cc66a-pugliellim]; Williams, Richard (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5f89fe4d27a43abb936bb20efeca3b9-rwilliams]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]
Subject: KEI Response Letter
Attachments: 2018-27674.pdf; Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan..pdf; Response to KEI J Love Comments_to DB and MR Jan 10.docx

Dear Dale and Mark,

We hope everything is going well with you.

As you know, we received comments from KEI/MSF to a recent FR Notice for an exclusive license to Medigen, a vaccine company in Taiwan this past week. KEI also contacted Senator Sanders' office, who is asking for a copy of the patent application and for NIH/NIAID to extend the comment period.

Attached please find our proposed response, the FR Notice, and KEI's comment letter.

Any input you could provide would be welcome.

b5

Please contact us if you have any additional questions. Thank you.

Peter Soukas
National Institutes of Health
National Institute of Allergy and Infectious Diseases
Phone: 301-594-8730
Email: ps193c@nih.gov

REL0000024483

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive Patent License: Production of Live Respiratory Syncytial Virus and Parainfluenza Virus Vaccines

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Institute of Allergy and Infectious Diseases, an institute of the National Institutes of Health, Department of Health and Human Services, is contemplating the grant of an Exclusive Commercialization Patent License to practice the inventions embodied in the Patents and Patent Applications listed in the Summary Information section of this notice to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

DATES: Only written comments and/or applications for a license which are received by the National Institute of Allergy and Infectious Diseases' Technology Transfer and Intellectual Property Office on or before January 7, 2019 will be considered.

ADDRESSES: Requests for copies of the patent application, inquiries, and comments relating to the contemplated Exclusive Commercialization Patent License should be directed to: Peter Soukas, Technology Transfer and Patent Specialist, Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 5601 Fishers Lane, Suite 6D, Rockville, MD 20852-9804; Email: ps193c@nih.gov; Telephone: (301) 496-2644; Facsimile: (240) 627-3117.

SUPPLEMENTARY INFORMATION:

Intellectual Property

U.S. Provisional Patent Application Number 62/661,320, filed April 23, 2018 and entitled "Chimeric Vaccines," [HHS Reference No. E-018-2018-0]; and U.S. and foreign patent applications claiming priority to the aforementioned applications.

The patent rights in this invention have been assigned to the Government of the United States of America.

The prospective exclusive licensed territory may be worldwide, and the field of use may be limited to: "Live Respiratory Syncytial Virus (RSV) and Parainfluenza Virus (PIV) vaccines."

Human respiratory syncytial virus (RSV) continues to be the leading viral cause of severe acute lower respiratory

tract disease in infants and children worldwide. A licensed vaccine or antiviral drug suitable for routine use remains unavailable. This invention relates to the use of murine pneumonia virus (MPV), a virus to which humans normally are not exposed and that is not cross-protected with RSV, as a vector to express the RSV fusion (F) glycoprotein as an RSV vaccine candidate. The RSV F ORF was codon optimized. The RSV F ORF was placed under the control of MPV transcription signals and inserted at the first (rMPV-F1), third (rMPV29 F3), or fourth (rMPV-F4) gene position of a version of the MPV genome that contained a codon pair optimized L polymerase gene. The recovered viruses replicated in vitro as efficiently as the empty vector, with stable expression of RSV F protein. Replication and immunogenicity of rMPV-F1 and rMPV-F3 were evaluated in rhesus macaques following administration by the combined intranasal and intratracheal routes. Both viruses replicated at low levels in the upper and lower respiratory tract, maintained stable RSV F expression, and induced similar high levels of RSV-neutralizing serum antibodies that reached peak titers by fourteen (14) days post-vaccination. rMPV provides a highly attenuated yet immunogenic vector for the expression of RSV F protein, with potential application in RSV-naïve and RSV experienced populations. The technology relates to live, chimeric non-human Mononegavirales vectors that allow a cell to express at least one protein from at least one human pathogen as well as compositions comprising the vectors, methods and kits for eliciting an immune response in a host, and methods of making the vectors.

This notice is made in accordance with 35 U.S.C. 209 and 37 CFR part 404. The prospective exclusive license will be royalty bearing, and the prospective exclusive license may be granted unless within fifteen (15) days from the date of this published notice, the National Institute of Allergy and Infectious Diseases receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR part 404.

Complete applications for a license in the prospective field of use that are timely filed in response to this notice will be treated as objections to the grant of the contemplated exclusive patent commercialization license. In response to this Notice, the public may file comments or objections. Comments and objections, other than those in the form of a license application, will not be

treated confidentially, and may be made publicly available. License applications submitted in response to this Notice will be presumed to contain business confidential information, and any release of information in these license applications will be made only as required and upon a request under the *Freedom of Information Act*, 5 U.S.C. 552.

Dated: December 11, 2018.

Suzanne M. Frisbie,

Deputy Director, Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases.

[FR Doc. 2018-27674 Filed 12-20-18; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Co-Exclusive Patent License: Production of Monovalent Live Attenuated Zika Vaccines and Multivalent Live Attenuated Zika and Dengue Vaccines

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Institute of Allergy and Infectious Diseases, an institute of the National Institutes of Health, Department of Health and Human Services, is contemplating the grant of a Co-Exclusive Commercialization Patent License to practice the inventions embodied in the Patents and Patent Applications listed in the Summary Information section of this notice to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan, and Panacea Biotech Ltd., having a place of business in New Delhi, India.

DATES: Only written comments and/or applications for a license which are received by the National Institute of Allergy and Infectious Diseases' Technology Transfer and Intellectual Property Office on or before January 22, 2019 will be considered.

ADDRESSES: Requests for copies of the patent application, inquiries, and comments relating to the contemplated Co-Exclusive Commercialization Patent License should be directed to: Peter Soukas, Technology Transfer and Patent Specialist, Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 5601 Fishers Lane, Suite 6D, Rockville, MD 20852-9804; Email:

January 7, 2018

Peter Soukas, J.D.
Technology Transfer and Patent Specialist
Technology Transfer and Intellectual Property Office
National Institute of Allergy and Infectious Diseases
National Institutes of Health, 5601 Fishers Lane, Suite 6D
Rockville, MD 20852-9804
Via Email: ps193c@nih.gov

Re: 83 FR 65696. Prospective Grant of Exclusive Patent License: Production of Live Respiratory Syncytial Virus and Parainfluenza Virus Vaccines to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

Dear Peter Soukas,

We are writing to express opposition to the grant of an exclusive license for U.S. Provisional Patent Application Number 62/661,320, filed April 23, 2018 and entitled "Chimeric Vaccines," [HHS Reference No. E-018-2018-0]; and U.S. and foreign patent applications claiming priority to the aforementioned application to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan.

According to the Federal Register notice 83 FR 65696, the intellectual property to be licensed is:

"U.S. Provisional Patent Application Number 62/661,320, filed April 23, 2018 and entitled 'Chimeric Vaccines,' [HHS Reference No. E-018-2018-0]; and U.S. and foreign patent applications claiming priority to the aforementioned applications."

A search for this application using several patent databases does not return any provisional application with that number. An email received on January 7, 2019, from Peter Soukas, J.D., to Knowledge Ecology International (KEI) confirmed that the patent application has not been published.

We note that the provisional application was filed in April 2018, and the USPTO normally does not publish such applications for 18 months, pursuant to 35 U.S.C. § 122.

KEI and Doctors without Borders/Médecins Sans Frontières (MSF) have asked your office for a copy of the patent application, but one was not provided.

Although the notice states that the license will also cover "foreign patent applications claiming priority to the aforementioned applications," and states that the geographical scope of the license "may be worldwide," the notice does not have information regarding which specific

countries will be included in this license. Because the provisional patent application was filed in April 2018, it is still well within the deadline to file for a PCT application or additional direct national filings. For the purpose of analysing the scope of a license and whether it complies with 35 U.S.C. § 209 and 37 CFR part 404, understanding which countries will be covered by the exclusive license is critically important. This information has not been provided.

The Federal Register notice 83 FR 65696 announcing the grant of this exclusive license was published on December 21, 2018, the Friday before the Christmas holiday. The deadline to file comments is January 7, 2019. While 35 U.S.C. § 209 states that public notice of the intention to grant an exclusive or partially exclusive license on a federally-owned invention has to be provided in an appropriate manner at least 15 days before the license is granted, the 15 days period is only a minimum. The NIH could grant a longer comment period, and in fact has done so with regards to other recent public notices.¹ There are no impediments to extending the deadline beyond the minimum of 15 days, and it would have been reasonable to do so given the limited amount of information provided in the notice.

According to the notice, the license will be granted to Medigen Vaccines Biologics Corp. (Medigen), having a place of business in Zhubei, Taiwan. On their website Medigen describes itself as, “an independent vaccine company developing vaccines against emerging infectious diseases and chronic diseases including cancer.”² Medigen was founded in 2004. The subsidiary based in Taiwan was founded in 2012.³ According to sbir.gov, Medigen has received \$ 4,632,774.00 in awards from HHS and the USDA.⁴

With regard to the invention, the Federal Register notice states the following:

“This invention relates to the use of murine pneumonia virus (MPV), a virus to which humans normally are not exposed and that is not cross-protected with RSV, as a vector to express the RSV fusion (F) glycoprotein as an RSV vaccine candidate.”

Despite the fact that the Federal Register notice provides limited information regarding the live respiratory syncytial virus, we believe this is an important virus affecting patients worldwide. According to T Shi, DA McAllister, KL O'Brien, et al., *Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study*, Lancet (2017):

“Globally, RSV is a common cause of childhood ALRI and a major cause of hospital admissions in young children, resulting in a substantial burden on health-care services.

¹ The Federal Register notice 83 FR 65696 related to a different exclusive license was also published by the NIH on December 21, 2018, but set a deadline to file comments until January 22, 2019.

² <https://www.federalregister.gov/d/2018-27672>

³ <https://medigen-usa.com/about/>

⁴ <http://www.medigen.com.tw/en/business-activities-medigen-vaccinology-corp/>

⁵ <https://www.sbir.gov/sbc/medigen-inc-0>

About 45% of hospital admissions and in-hospital deaths due to RSV-ALRI occur in children younger than 6 months. An effective maternal RSV vaccine or monoclonal antibody could have a substantial effect on disease burden in this age group.”

According to Graham, Barney S. *Vaccines against respiratory syncytial virus: The time has finally come*, Vaccine vol. 34,30 (2016): 3535-41:

“Respiratory syncytial virus (RSV) is the most common cause of hospitalization in children under 5 years of age. In developing countries RSV also causes substantial mortality in children under 1 year of age. All children are infected by the age of 3 and people are repeatedly infected throughout life. In otherwise healthy children over 5 years of age and in adults, RSV typically causes an upper respiratory syndrome sometimes complicated by sinusitis and otitis media. In individuals with T cell deficiencies like Severe Combined Immunodeficiency (SCID) or following allogeneic bone marrow transplantation or lung transplantation, RSV can cause a life-threatening progressive pneumonia. In addition, RSV infection in the frail elderly is associated with excess mortality at frequencies comparable to influenza virus infection. Infections tend to be seasonal in temperate climates, but in tropical climates can be detected throughout the year.”

“Approximately 20 per 1000 infants less than six months of age are hospitalized with severe RSV illness, and in the institutionalized elderly about 1–2 per 1000.”

The Federal Register notice provides almost no information on parainfluenza, or why this virus will also be covered by the license, but we believe that this is also a virus with an important global disease burden. According to Sato M, Wright PF. *Current status of vaccines for parainfluenza virus infections*, *Pediatr Infect Dis J.* (2008) October 27 (10 Suppl):S123-5:

“Because PIVs account for 17% of hospitalized illness associated virus isolation, the development of PIV vaccine would be a major advance in preventing lower respiratory tract infection in infants and young children.”

In the event that the NIH decides to grant this exclusive license to a company based in Zhubei, Taiwan, we ask that the following safeguards be placed on the license.

1. Any vaccine using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard.
2. The exclusive license does not extend to countries with a per capita income less than 30 percent of the United States, in order to ensure that the patents do not lead to restricted and unequal access in developing countries.

3. Medigen must agree to disclose the steps it will take to enable the timely registration and availability of the vaccine at an affordable price in the United States and in every county with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC)/ World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.
4. The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the vaccine from competitive suppliers, including technology transfer, in developing countries, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the vaccine.
5. Reduce term of exclusivity when revenues are large. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. This request is consistent with the statutory requirements of 35 USC § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” There are a number of ways the NIH could implement this in practice. We would be pleased to discuss ideas further.
6. The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Conclusion

We object to the grant of an exclusive patent license and urge the United States government to consider the negative impact an exclusive agreement will have on the development, affordability and availability of potential RSV or parainfluenza virus vaccines for people affected by these viruses in the United States and worldwide.

1. There is a lack of transparency regarding the proposed technology to be licensed, and the extent the public sector has already and will going forward subsidize the development of one or more vaccines covered by the license. The patent application is not public.
2. The notice period covering 10 business days and two public holidays including Christmas and New Years Day is insufficient time to evaluate the potential of the technology included in the license and the impact an exclusive license may have on ensuring appropriate further development of resulting candidate vaccines, or access and affordability of resulting vaccine products.
3. The NIH has not provided any information to establish that there is an appropriate justification for the grant of an exclusive license, and if so, that the scope of the rights granted have been limited to that which is reasonably necessary, under the standards set out in 35 U.S.C. § 209.
4. If the NIH does proceed with an exclusive license, the license should at a minimum include provisions to safeguard affordable access, and limit the scope of the exclusive rights to those reasonably necessary to induce the necessary investment to bring the inventions into practical application, as defined in 35 U.S.C. § 201(f).

Based upon the objections described herein, and the lack of sufficient information provided in the Federal Register notice, we request that the NIH consider a non-exclusive license or provide additional information relevant to evaluating this proposed licensing agreement and provide opportunities to consider the proposed license based on this information through a hearing or subsequent comment period.

Sincerely,

Knowledge Ecology International (KEI)

Doctors Without Borders/Médecins Sans Frontières USA



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health/ NIAID

5601 Fishers Lane
Rockville, MD 20852
Suite 6D, MSC 9804
Tel (301) 496-2644

DRAFT

James Love
Director, Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
+1.202.332.2670
james.love@keionline.org

Subject: Comments Submitted in Response to Federal Register Notice 2018-65696 (83 FR 65696), entitled
“Prospective Grant of Exclusive Patent License: Production of Live Respiratory Syncytial Virus and
Parainfluenza Virus Vaccines”

Dear Mr. Love:

b5

Sincerely,

Technology Transfer and Patent Specialist

REL0000024483.0003

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 12/14/2018 7:37:50 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Knabb, Jim (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=535517d229e04963a2b928742cb80da0-knabbjr]
Subject: RE: Do know of a way to search TTS for any licenses with comments from KEI?

To my knowledge, NCI has been attaching these communications in TT and so you would need to be able to search the attached files. I don't know if you can do that and that would be a question for Tim Leahy or Steve Finley. I think we used to be able to do that but I'm not sure.

Richard

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, December 14, 2018 1:33 PM
To: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: RE: Do know of a way to search TTS for any licenses with comments from KEI?

Looking for total number rather than content

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, December 14, 2018 1:32 PM
To: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: Do know of a way to search TTS for any licenses with comments from KEI?

..other than one by one.

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/20/2018 3:47:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: KEI suing NIH over CAR-T license

This certainly ups the ante

(<https://www.keionline.org/27669>):

KEI sues NIH over license of CD30 CAR T patents to Gilead

Posted on April 19, 2018 by James Love

On April 19, 2018, KEI filed a lawsuit against the National Institutes of Health (NIH) to block or invalidate an exclusive license of patents on a new chimeric antigen receptor T-cell (CAR T) therapy to Gilead Sciences. A copy of the complaint is available here:

[KEIvNIH09319352421](#)

The license in question involves a set of patent applications regarding the development of a CD30 chimeric antigen receptor (CAR)-based immunotherapy using autologous (meaning one individual is both the donor and the recipient) T-cells, for the treatment of:

- Hodgkin lymphoma (HL),
- Non-Hodgkin's Lymphoma (NHL),
- diffuse large B cell lymphoma (DLBCL),
- peripheral T cell lymphoma not otherwise specified (PTCL-NOS),
- anaplastic large cell lymphoma (ALCL), and
- angioimmunoblastic T cell lymphoma (AITL).

The complaint stems from (1) the NIH's refusal to entertain an appeal from KEI on its intention to proceed with the proposed license even prior to KEI submitting the appeal itself, and (2) the self-proclaimed assertion by NIH that it is exempt from the requirement under 40 U.S.C. § 599 that creates a black letter obligation on federal agencies to seek the antitrust advice of the Attorney General prior to the disposal of federal property.

The complaint asserts that these acts constitute violations of the relevant law and regulations, including the Administrative Procedure Act.

The lawyers for KEI were Andrew Goldman of KEI, and Daniel Doty, an attorney in private practice in Baltimore.

For some additional context, see:

2018. January 5. Briefing note on NIH proposed license to Gilead for CD-30 CAR T technology,
KEIOnline.Org

2018. February 27. KEI Appeals NIH/NCI Decision to Proceed with License of CD30 CAR T technology to Gilead/Kite, KEIOnline.Org

Note also that last year Gilead paid \$11.9 billion to buy Kite Pharma, whose main assets were CD19-directed genetically modified autologous T-cell immunotherapy patents licensed from the NIH, and Celgene recently spent \$9 billion to buy Juno Therapeutics, whose main assets were also CAR T technologies also invented on NIH grants. In the current case the NIH is giving Gilead an exclusive license on CD30-directed genetically modified autologous T-cell immunotherapy patents, on the cheap, with no requirements on pricing or access.

Note further than the prices for the first two CAR T treatments (\$475,000 for Kymriah and \$373,000 for Yescarta) were so high that access has been limited.

Access to Medicine, Competition, Government Funded research Gilead Sciences, NIH

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Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
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www.allen-assoc.com

From: Freel, Rose (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E8AE9AAB7E3249E881BB573E9A189036-FREELRM]
Sent: 7/23/2018 6:07:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.
Attachments: KEIComments_DRAFTresponse_7.20.2018.doc

Hi Mark & Dale,

I've put together a draft response to KEI's comments. Could you please look at the attached and let me know any edits or comments?

Thanks!

Rose

--

Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 2:55 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

I agree with Dale with a suggestion.

b5

b5

From: Freel, Rose (NIH/NCI) [E]
Sent: Thursday, July 19, 2018 8:05 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Just following up on this, let me know your thoughts on a response to KEI.

Thanks!

Rose

--

REL0000024490

Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Freel, Rose (NIH/NCI) [E]
Sent: Tuesday, July 17, 2018 8:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Attached are comments I received from KEI on the FR Notice for the Prospective Grant to Atara. Can you please tell me if and how we should respond?

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: James Love <james.love@keionline.org>
Sent: Friday, July 13, 2018 4:45 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Tim Reed <Tim@haiweb.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Alex Lawson <alawson@socialsecurityworks.org>; Fran Quigley <b6> Baker, Brook <b.baker@northeastern.edu>; Meg Jones-Monteiro <mjonesmonteiro@iccr.org>; Manon Ress <MANON.RESS@cancerunion.org>; Claire Cassedy <claire.cassedy@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Freel,

I'm attaching a corrected copy of the comments. The difference was just the spelling of CFR, which had been transposed in the earlier version.

Jamie

On Fri, Jul 13, 2018 at 4:09 PM, James Love <james.love@keionline.org> wrote:

Dr. Freel,

Attached are comments on the Atara license from:

Health Action International (HAI)
Health GAP
Interfaith Center on Corporate Responsibility (ICCR)

REL0000024490

Knowledge Ecology International (KEI)
People of Faith for Access to Medicines (PFAM)
Social Security Works (SSW)
Union for Affordable Cancer Treatment (UACT)
Universities Allied for Essential Medicines (UAEM)

James Love, Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

James Love, Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love



National Institutes of Health
National Cancer Institute
Technology Transfer Center
8490 Progress Drive
Riverside 5 building, Suite 400
Frederick, MD 21701
Phone (301) 624-8775
FAX (301) 631-3033

via email only

July 20, 2018

James Love
Knowledge Ecology International (KEI)
1621 Connecticut Avenue, Suite 500,
Washington DC 20009

RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin
Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer (83 FR 30448)

Dear Mr. Love,

b5

Sincerely,

Rose M. Freel, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/21/2018 1:45:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Rydapt - failure to disclose federal funding

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 9:45 AM
To: 'Andrew Goldman' <andrew.goldman@keionline.org>
Cc: Jamie Love <james.love@keionline.org>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: Rydapt - failure to disclose federal funding

Dear Andrew:

Thank you for forwarding KEI's documentation concerning Rydapt. NIH will review the issues and questions you have raised and will provide you with its response.

Ann Hammersla

Ann M. Hammersla, J.D.
Director,
Division of Extramural Research Resources

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]
Sent: Wednesday, March 21, 2018 8:09 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: Re: Rydapt - failure to disclose federal funding

Dear Ann:

Thank you for your reply. Attached please find five pdf documents concerning the Rydapt issue I mentioned yesterday:

- (1) a brief cover letter regarding the Rydapt issue;
- (2) the memorandum on the failure to disclose (Rydapt-james-griffin-dana-farber-novartis-21Mar2018);
- (3) ANNEX: James Griffin's 71 NIH Funded Projects (ANNEX-james-griffin-NIH-RePORTer-20March2018);
- (4) ANNEX: Griffin's CA36167 Grants, from NIH REPORTER (ANNEX-griffin-CA36167-NIH-REPORTER)
- (5) ANNEX: KEI-Briefing-Note-2018-1

Thank you for your attention to this matter.

Sincerely,
Andy

--
Andrew S. Goldman
Counsel, Policy and Legal Affairs

REL0000024493

Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

On Tue, Mar 20, 2018 at 3:27 PM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

Dear Andrew:

Thank you for your courtesy notice that KEI is submitting a new request asking the NIH to take ownership actions for Rydapt.

NIH will review the Rydapt request and NIH's funding, if any, and is now reviewing the earlier requests you have submitted and will you and KEI know the results of NIH's internal research.

Ann

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

From: Andrew Goldman <andrew.goldman@keionline.org>

Sent: Tuesday, March 20, 2018 1:22 PM

To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>

REL0000024493

Cc: Jamie Love <james.love@keionline.org>

Subject: Rydapt - failure to disclose federal funding

Dear Dir. Hammersla:

I wanted to provide you a courtesy notice that we are finalizing a document similar to the two we have sent in recent days, this time requesting that NIH conduct an investigation into the failure to disclose federal funding leading to the expensive medicine Rydapt (INN midostaurin). The document requests that NIH remedy that failure by taking title to the patents at issue. The memorandum and appendices will detail the grants issued to inventor James Griffin, and their relationship to the patents.

Kind regards,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: [+1.202.332.2670](tel:+12023322670)

www.keionline.org

From: Vepa, Sury (NIH/NCATS) [E] [/O=NIH/OU=EXTERNAL (FYDIBOHF25SPDLT)/CN=RECIPIENTS/CN=CE576258D4054767B9B2279A8FCD32E4]
Sent: 7/17/2017 4:03:24 PM
To: Burgoon, Penny (NIH/NCATS) [E] [/O=NIH/OU=EXtErnal (FYDIBOHF25SPDLT)/cn=Recipients/cn=f000ebe6ac674035a6cb04458d5cef41]; Portilla, Lili (NIH/NCATS) [E] [/O=NIH/OU=EXtErnal (FYDIBOHF25SPDLT)/cn=Recipients/cn=1d3dbcee212e4583a0262200948735b6]; Seidel, Stephen (NIH/NCATS) [E] [/O=NIH/OU=EXtErnal (FYDIBOHF25SPDLT)/cn=Recipients/cn=109885dc92e64b8194dfbbbd527f723d]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors

Hi Mark,

As you know previously, we received a query and a comment from James Love of KEI in response to our FR Notice for an exclusive license.

Based on your and Dave Lambertson's input (Dave has responded to a similar query from KEI for one of his licenses) and discussion with Lili, I drafted the response below.

Please let me know your suggestions and I am planning to send our response as soon as I have your and NCATS policy feedback.

Thanks,

Sury

Hi Lili,

Based on the input that I received from Mark Rohrbaugh and Dave Lambertson (who previously responded to KEI on a similar matter), below is my draft response to KEI.

Please let me know your suggestions and then I will send them to Mark and NCATS Policy (Penny and Steve Sidel) for their input and review.

Thanks,

Sury

Dear Mr. Love,

b5

b5

Sury Vepa
301-217-9197
(b6)(cell)

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From: Burgoon, Penny (NIH/NCATS) [E]
Sent: Friday, June 2, 2017 8:25 AM
To: Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>; McInnes, Pamela (NIH/NCATS) [E] <pmcinnnes@mail.nih.gov>; Seidel, Stephen (NIH/NCATS) [E] <SeidelS@mail.nih.gov>
Cc: Austin, Christopher (NIH/NCATS) [E] <austinc@mail.nih.gov>; Simeonov, Anton (NIH/NCATS) [E] <asimeono@mail.nih.gov>; Knebel, Ann (NIH/NCATS) [E] <ann.knebel@nih.gov>; Balakrishnan, Krishna (NIH/NCATS) [E] <Krishna.Balakrishnan@nih.gov>; Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors

Thanks Lili,

Please loop in Steve Seidel on this.

Penny

From: Portilla, Lili (NIH/NCATS) [E]
Sent: Wednesday, May 31, 2017 5:18 PM
To: McInnes, Pamela (NIH/NCATS) [E] ; Burgoon, Penny (NIH/NCATS) [E]
Cc: Austin, Christopher (NIH/NCATS) [E] ; Simeonov, Anton (NIH/NCATS) [E] ; Knebel, Ann (NIH/NCATS) [E] ; Balakrishnan, Krishna (NIH/NCATS) [E] ; Vepa, Sury (NIH/NCATS) [E]
Subject: FW: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors
Importance: High

Dear Penny and Pamela:

Sury received the email below from Jamie Love's organization Knowledge Ecology International (KEI) They found a pre-publication Federal Register Notice for the IDH1 inhibitor compound that we contemplate to exclusively license to GeneXion Oncology. This company submitted a license application about 6 weeks ago.

<https://s3.amazonaws.com/public-inspection.federalregister.gov/2017-11241.pdf> Please note that the same notice will "officially" publish tomorrow in the Federal Register.

Sury will be contacting Mark Rohrbaugh at NIH OSP about this matter on how best to proceed with a response to this group. Mark is very familiar with Mr. Love's organization. Please note that KEI has been sending similar inquires to other ICs exclusively licensing NIH patents. Penny, please let us know if you or someone else in your group should be involved in these discussions.

Thanks,

Lili

REL0000024494

From: Vepa, Sury (NIH/NCATS) [E]
Sent: Wednesday, May 31, 2017 2:44 PM
To: Balakrishnan, Krishna (NIH/NCATS) [E] <Krishna.Balakrishnan@nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: FW: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors

Hi Lili,

Please see an email from KEI in response to the IDH1 FR Notice.

Thanks,

Sury

Sury Vepa
301-217-9197
b6 (cell)

This e-mail may contain confidential and/or privileged material for the sole use of the intended recipient. Any review or distribution by others is strictly prohibited. If you are not intended recipient please contact the sender and delete all copies of this e-mail.

From: jamespackardlove@gmail.com [mailto:jamespackardlove@gmail.com] **On Behalf Of** Jamie Love
Sent: Wednesday, May 31, 2017 12:43 PM
To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>
Cc: Diane Singhroy <diane.singhroy@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Andrew S. Goldman <andrew.goldman@keionline.org>
Subject: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors

Sury Vepa, Ph.D., J.D.,
Senior Licensing and Patenting Manager
National Center for Advancing Translational Sciences'
NIH, 9800 Medical Center Drive, Rockville, MD 20850,
Phone: 301-217-9197,
Fax: 301-217-5736,
email sury.vepa@nih.gov.

Dear Dr. Vepa,

1. We propose there be language in the license to ensure that prices for products are "reasonable" -- the standard in 35 U.S.C. § 201(f) -- and do not discriminate against U.S. residents.

One very basic protection for US. residents is to ensure that prices are not higher than the median price of other high income industrialized countries.

For example, the license could say:

The [agency] will normally expect the licensee to make products available to the public in the United States at prices no higher than the median price charged in the seven countries with the largest GDP, that have per capita incomes of at least half that of the United States.

We may propose additional pricing safeguards later, including to address access in developing countries.

2. We would like to learn more about the technology being licensed. Could we set up a call with myself, Diane Singhroy and persons at the NIH who can answer questions about the technology and the NIH role in its funding?

James Love
KEI

--

James Love. Knowledge Ecology International

<http://www.keionline.org/donate.html>

KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,

twitter.com/jamie_love

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 12/14/2018 7:40:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: [REDACTED] b5 before Christmas week?

Great, thanks!

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, December 14, 2018 11:40 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: [REDACTED] b5 before Christmas week?

Yes, I am here through Thursday.

[REDACTED] b5

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Friday, December 14, 2018 11:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: [REDACTED] b5 before Christmas week?

Mark:

[REDACTED]

b5

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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REL0000024498

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/21/2018 1:45:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Rydapt - failure to disclose federal funding

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, March 21, 2018 9:18 AM
To: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Cc: Jackson, Stephanie (NIH/OD) [C] <stephanie.jackson3@nih.gov>
Subject: FW: Rydapt - failure to disclose federal funding

Michelle:

NIH has received 3 march-in requests over the past 2 weeks. In addition the

b5

b5

Ann

From: Andrew Goldman [mailto:andrew.goldman@keionline.org]
Sent: Wednesday, March 21, 2018 8:09 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: Re: Rydapt - failure to disclose federal funding

Dear Ann:

Thank you for your reply. Attached please find five pdf documents concerning the Rydapt issue I mentioned yesterday:

- (1) a brief cover letter regarding the Rydapt issue;
- (2) the memorandum on the failure to disclose (Rydapt-james-griffin-dana-farber-novartis-21Mar2018);
- (3) ANNEX: James Griffin's 71 NIH Funded Projects (ANNEX-james-griffin-NIH-RePORTer-20March2018);
- (4) ANNEX: Griffin's CA36167 Grants, from NIH REPORTER (ANNEX-griffin-CA36167-NIH-REPORTER)
- (5) ANNEX: KEI-Briefing-Note-2018-1

Thank you for your attention to this matter.

REL0000024502

Sincerely,
Andy

--

Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

On Tue, Mar 20, 2018 at 3:27 PM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

Dear Andrew:

Thank you for your courtesy notice that KEI is submitting a new request asking the NIH to take ownership actions for Rydapt.

NIH will review the Rydapt request and NIH's funding, if any, and is now reviewing the earlier requests you have submitted and will you and KEI know the results of NIH's internal research.

Ann

--

Ann M. Hammersla, J.D.

Director

Division of Extramural Inventions and Technology Resources

Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310

6705 Rockledge Drive

Bethesda, Maryland 20892-7974

PHONE: 301-435-0745

REL0000024502

From: Andrew Goldman <andrew.goldman@keionline.org>
Sent: Tuesday, March 20, 2018 1:22 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>
Subject: Rydapt - failure to disclose federal funding

Dear Dir. Hammersla:

I wanted to provide you a courtesy notice that we are finalizing a document similar to the two we have sent in recent days, this time requesting that NIH conduct an investigation into the failure to disclose federal funding leading to the expensive medicine Rydapt (INN midostaurin). The document requests that NIH remedy that failure by taking title to the patents at issue. The memorandum and appendices will detail the grants issued to inventor James Griffin, and their relationship to the patents.

Kind regards,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: [+1.202.332.2670](tel:+12023322670)

www.keionline.org

From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 8/15/2017 9:01:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: NEED FEDBACK BY TOMORROW PLEASE

Hi Mark,

Carrie was **b6** today. If you have not received a response by early morning, I would send this again with (PLSRD!) in the subject line.

Best!
Ashley

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, August 15, 2017 2:24 PM
To: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>
Cc: Parker, Ashley (NIH/OD) [E] <ashley.parker@nih.gov>
Subject: NEED FEDBACK BY TOMORROW PLEASE

Carrie:

The NCI Fed Reg. notice of intent to grant an exclusive license to Salubris for the cancer indication expires Monday after 15 days of posting. Staffers from Sen Sanders and Durbin have been in touch with Laura Berkson to raise concerns based on the news article. **b5**

b5

b5

Are you ok with this?

Thanks,
Mark

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

REL0000024503

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/10/2019 5:38:03 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: KEI Response to Jasmine's FRN
Attachments: Ltr to KEI_2019-01-09_RL2_1-10-19--OGCBerkleyComments.docx

I would do something like in the attached, for your consideration.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 11:35 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: KEI Response to Jasmine's FRN

The question I had was: b5

b5

From: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Sent: Thursday, January 10, 2019 11:32 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: KEI Response to Jasmine's FRN

Let me take a look at it now...

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Thursday, January 10, 2019 11:31 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: FW: KEI Response to Jasmine's FRN

I am going to suggest: b5
OK with this version?

From: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Sent: Thursday, January 10, 2019 9:00 AM

REL0000024504

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>

Cc: Yang, Jasmine (NIH/NCI) [E] <jasmine.yang@nih.gov>; Thomas, Jeffrey (NIH/NCI) [E] <jeffreyt@mail.nih.gov>

Subject: KEI Response to Jasmine's FRN

Hi Mark,

b5

b5

Please let us know if you have additional thoughts.

Thanks,

Richard

RICHARD U. RODRIGUEZ
Associate Director
Patent Agent

Technology Transfer Center
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<https://techtransfer.cancer.gov>

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

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REL0000024504

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From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 10/18/2017 7:44:52 PM
To: Myles, Renate (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7d317f5626934585b3692a1823c1b522-mylesr]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Fine, Amanda (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=61290b74aa9a44358954c45439ffdeb6-fineab]
CC: Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]; Bulls, Michelle G. (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b366f1a4382d44c1bde626e7730c3dd4-bullsmg]; Jackson, Stephanie (NIH/OD) [C] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=813a0dc9ddbc4fa2be8ca6ea23d081ca-jacksonsg]
Subject: RE: question from a journalist

All:

The request from KEI does ask NIH to use its march-in rights. KEI requests a meeting with the Secretary based on its erroneous analysis that the University of Pennsylvania did not disclose to NIH its CAR T subject inventions and that the filed US patents do not cite NIH funding.

Ann

From: Myles, Renate (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 3:17 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: question from a journalist

Hi Mark:

What Amanda is asking is:

b5

b5

Thanks,

Renate

REL0000024508

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 3:02 PM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: question from a journalist

b5

From: Fine, Amanda (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 2:50 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: question from a journalist

Hi All-

Just following up about

b5

b5

Thanks!
Amanda

From: Fine, Amanda (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 4:56 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: question from a journalist

Hi Ann-

Just to update you,

b5

b5

Thanks again for your help!
Amanda

From: Fine, Amanda (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 12:05 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E]

REL0000024508

<RohrBauM@OD.NIH.GOV>

Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>

Subject: RE: question from a journalist

Hi Ann-

Thanks for this information.

b5

b5

Thanks again!

Amanda

From: Hammersla, Ann (NIH/OD) [E]

Sent: Tuesday, October 17, 2017 11:32 AM

To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>

Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>

Subject: RE: question from a journalist

Hello Amanda:

OPERA/DETR is reviewing KEI's 10/16/2017 letter re the CR T technology. Please let me know:

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b5

Note the KEI

letter is not requesting a march-in but outlining in significant detail about what it has determined to be non-compliance of the University of Pennsylvania.

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]

Sent: Tuesday, October 17, 2017 11:08 AM

To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>

Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>

Subject: FW: question from a journalist

b5

REL0000024508

From: Fine, Amanda (NIH/OD) [E]
Sent: Tuesday, October 17, 2017 10:44 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: FW: question from a journalist

Hi Mark-

ASPA forwarded the below inquiry from Ed Silverman about the attached KEI letter to the Secretary about patents to CAR T technologies used by UPenn researchers. KEI's letter asks for an investigation because it claims that these PIs didn't mention NIH/federal funding or that the technologies included NIH patented inventions.

b5

Please let me know if you need any additional information.

Thanks!
Amanda

From: OS Media (HHS/ASPA) [<mailto:media@hhs.gov>]
Sent: Tuesday, October 17, 2017 10:04 AM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Cc: OS Media (HHS/ASPA) <media@hhs.gov>
Subject: FW: question from a journalist

From: Silverman, Ed [<mailto:ed.silverman@statnews.com>]
Sent: Tuesday, October 17, 2017 9:56 AM
To: OS Media (HHS/ASPA)
Subject: question from a journalist

Hi

My name is Ed Silverman and I run the Pharnalot blog at The Boston Globe's STAT health and medicine site.

An advocacy group called Knowledge Ecology International wrote the HHS yesterday, alleging that the University of Pennsylvania failed to disclose that five patents for a particular cancer treatment called CAR-T were developed with federal funds provided by NIH.

The group wrote to Acting Secretary Hargan that "the Bayh-Dole Act requires that companies disclose when public funds are used to create an invention. These disclosures should be made on the application for the patent and printed on the patent in a "Statement Regarding Federally Sponsored Research Or Development."

Their letter is attached.

The HHS was asked to investigate and I would like to know if an investigation will be undertaken to determine whether the disclosure was made appropriately or not.

REL0000024508

Thanks,
Ed Silverman
973-493-7851
www.statnews.com/pharmalot/

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 1/10/2019 5:53:55 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Stackhouse, Thomas (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7e1c23441b64258803cab5e97db8270-stackhot]; Ferguson, Steve (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aec79b088ce947819eadd4bf420aa54b-fergusos]; Bradley, David (NIH/NIDCR) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4232ab2d5334498ba86abbcec1e39784-bradleyda]
Subject: RE: How Shutdown is affecting NIH Exclusive Licensing

Ah, that is a good point I hadn't considered. Well, it was a thought.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, January 10, 2019 12:52 PM
To: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Bradley, David (NIH/NIDCR) [E] <david.bradley@nih.gov>
Cc: Stackhouse, Thomas (NIH/NCI) [E] <stackhot@otd.nci.nih.gov>; Ferguson, Steve (NIH/OD) [E] <FERGUSOS@od6100m1.od.nih.gov>
Subject: RE: How Shutdown is affecting NIH Exclusive Licensing

The federal register has been around since 1936. Pre-Steve I hope. ☺

The regs were changed last year to allow us to use other means of broad publication but I would

b5

b5

From: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Sent: Thursday, January 10, 2019 12:46 PM
To: Bradley, David (NIH/NIDCR) [E] <david.bradley@nih.gov>
Cc: Stackhouse, Thomas (NIH/NCI) [E] <stackhot@otd.nci.nih.gov>; Ferguson, Steve (NIH/OD) [E] <fergusos@od6100m1.od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: How Shutdown is affecting NIH Exclusive Licensing

I don't know what was done before the Federal Register. Perhaps ask Steve Ferguson?

b5

I decided to copy both so let's see what they say.

Richard

From: Bradley, David (NIH/NIDCR) [E]
Sent: Thursday, January 10, 2019 12:42 PM
To: Stackhouse, Thomas (NIH/NCI) [E] <stackhot@otd.nci.nih.gov>; Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: RE: How Shutdown is affecting NIH Exclusive Licensing

I was looking at 35 USC 209(e) today and it says no license may be granted unless the intention has been provided in an "appropriate manner". I wonder if

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REL0000024511

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Richard, do you know how notices were handled back in the early days of tech transfer? I wonder if

b5

b5

David William Bradley, Ph.D.
Director, Office of Technology Transfer and Innovation Access (OTTIA)
National Institute of Dental and Craniofacial Research (NIDCR)
BLDG 1DEM RM 687-K
6701 DEMOCRACY BLVD, MSC 4878
BETHESDA MD 20817-4878
bradleyda@nidcr.nih.gov
954.435.4824

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NIDCR Staff, please submit New Tech Transfer Requests through our website:

<https://nidcrintranet.nidcr.nih.gov/DIR/OSD/techtransfer/datalink/Site%20Pages/TTServiceRequests-Requesters.aspx>

From: Stackhouse, Thomas (NIH/NCI) [E]
Sent: Thursday, January 10, 2019 12:29 PM
To: OD-OTT-TDC-10 <ODOTTDC10@mail.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: FW: How Shutdown is affecting NIH Exclusive Licensing

Hello All:

NCI is gathering information regarding the negative ripple effect the current partial gov't furlough is having on our NCI programs

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TTC will be sending the following note to our NCI leadership

b5

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Please check with your staff and let me know of any today, if possible.

Thanks!
Tom

Thomas M. Stackhouse, Ph.D.
Director, Technology Transfer Center
National Cancer Institute, NIH, DHHS
301-624-1245

"Engaged partnerships benefiting research, innovation and public health."

REL0000024511

From: Rodriguez, Richard (NIH/NCI) [E]
Sent: Thursday, January 10, 2019 10:47 AM
To: Stackhouse, Thomas (NIH/NCI) [E] <stackhot@otd.nci.nih.gov>
Subject: How Shutdown is affecting NIH Exclusive Licensing

Tom,

As requested:

- NIH ICs are required to post public notices in the Federal Register for a period of 15 days regarding the intent to grant exclusive licenses. These notices invite public comment [b5]
[b5] The negotiations of these exclusive licenses cannot proceed without this public notice period. Due to the partial Government shutdown, no Federal Register notices are being published. [b5]
[b5]

RICHARD U. RODRIGUEZ
Associate Director
Patent Agent

Technology Transfer Center
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive, Rm 1E530
Bethesda, MD 20892-9702 (for business mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Phone (Main Office): 240-276-5530
Direct phone: 240-276-6661
Fax 240-276-5504
richard.rodriguez@nih.gov
<https://techtransfer.cancer.gov>

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

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REL0000024511

From: Knabb, Jim (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=535517D229E04963A2B928742CB80DA0-KNABBJR]
Sent: 12/12/2018 5:54:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Comments on NIH Prospective License CAR Therapies to ElevateBio - 83 FR 58262
Attachments: 83FR58262_Comments_NIH_ElevateBIO_4Nov2018.pdf

Mark,

Attached are the comments from KEI on the recent proposed license to ElevateBio. I had presumed that you saw the comments as they were posted publicly on the KEI website. If I presumed incorrectly I apologize for not sending them to you sooner.

We've discussed this at NCI [REDACTED] b5 I'm happy to discuss with you if you feel otherwise.

Best,
Jim

From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Tuesday, December 04, 2018 9:53 PM
To: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>
Cc: James Love <james.love@keionline.org>; Alex Lawson <alawson@socialsecurityworks.org>; Manon Ress <manon.ress@keionline.org>; Peter Maybarduk <pmaybarduk@citizen.org>; Baker, Brook <b.baker@northeastern.edu>; Ophira Ginsburg <ophiraginsburg@gmail.com>
Subject: Re: Comments on NIH Prospective License CAR Therapies to ElevateBio - 83 FR 58262

Dear Mr. Knabb,

Please find attached a revised edition of the comments, which includes an additional signatory, Dr. Ophira Ginsburg. Thank you.

Sincerely,
Claire Cassedy

--
Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

On Tue, Dec 4, 2018 at 9:23 PM Claire Cassedy <claire.cassedy@keionline.org> wrote:

Dear Jim Knabb,

Please find attached comments submitted on behalf of Knowledge Ecology International (KEI), the Union for Affordable Cancer Treatment (UACT), Social Security Works (SSW), Health GAP, Public Citizen, and James Love, in response to Federal Register notice 83 FR 58262, "Prospective Grant of an Exclusive Patent License:

REL0000024513

Development and Commercialization of Chimeric Antigen Receptor (CAR) Therapies for the Treatment of FMS-Like Tyrosine Kinase 3 (FLT3) Expressing Cancers." Thank you for your consideration.

Sincerely,
Claire Cassedy

--
Claire Cassedy
Knowledge Ecology International
1621 Connecticut Avenue NW
Suite 500
Washington, DC 20009
Tel.: 1.202.332.2670

November 4, 2018

Jim Knabb
Senior Technology Transfer Manager
NCI Technology Transfer Center
Email: jim.knabb@nih.gov

Re: Prospective Grant of an Exclusive Patent License to ElevateBio

Dear Jim Knabb,

The following are comments by Knowledge Ecology International (KEI), the Union for Affordable Cancer Treatment (UACT), Social Security Works (SSW), Health GAP, Public Citizen, Ophira Ginsburg, and James Love regarding the "Prospective Grant of an Exclusive Patent License: Development and Commercialization of Chimeric Antigen Receptor (CAR) Therapies for the Treatment of FMS-Like Tyrosine Kinase 3 (FLT3) Expressing Cancers," to ElevateBio, as noticed in the Federal Register notice [83 FR 58262](#).

Table of Contents

Inventions to be licensed	2
Global Incidence of Leukemia	2
40 USC § 599	6
The process has lacked transparency	6
The key figures in ElevateBio have a record of aggressively pricing drugs	6
Low- and middle-income countries	8
Designated Countries	8
MPP	9
Definitions of countries with access challenges	9
35 USC § 209	9
35 USC § 201(f) – definition of practical application	10
Proposals for safeguards to protect the public's rights in the patented inventions	10
No discrimination against U.S. residents in pricing	10
Additional provisions on affordability	11

Reduce term of exclusivity when revenues are large	11
Test data	11
Transparency	12

Inventions to be licensed

E-133-2016: FLT3-Specific Chimeric Antigen Receptors and Methods Using Same

1. US Provisional Patent Application 62/342,394, filed May 27, 2016 (E-133-2016-0-US-01);
2. International Patent Application PCT/US2017/034,691, filed May 26, 2017 (E-133-2016-0-PCT-02)

“The development of a mono- or multi-specific FMS-like tyrosine kinase 3 (FLT3; also known as CD135) chimeric antigen receptor (CAR)-based immunotherapy using autologous or allogenic human lymphocytes (T cells or NK cells) transduced with lentiviral vectors, wherein the viral transduction leads to the expression of a CAR that targets FLT3 (comprised of the FLT3-binding domain referenced as NC7 in the invention as well as an intracellular signaling domain), for the prophylaxis or treatment of FLT3-expressing cancers.”

This technology discloses a CAR vector that targets FLT3 comprised of an anti-FLT3 antibody known as NC7, and an intracellular signaling domain. FLT3 (CD135) is a cytokine receptor expressed on hematopoietic progenitor cells, and is one of the most frequently mutated genes in acute myeloid leukemia (AML) and infant acute lymphoblastic leukemia (ALL). FLT3 mutation leads to increased cell surface expression and therefore on leukemic cells, which makes it an attractive candidate for cellular therapies such as CAR-T.

Global Incidence of Leukemia

According to the US Centers for Disease Control and Prevention (CDC), "Acute lymphoblastic leukemia (ALL) is the most prevalent cancer among children and adolescents in the United States, representing 20% of all cancers diagnosed in persons aged <20 years."¹

Globally, the U.S. has a relatively high rate of incidence of leukemia in general, and AML and ALL in particular, but the bulk of the cases are outside the United States.

The following data are a table and two figures from: “Epidemiological patterns of leukaemia in 184 countries: a population-based study.” The Lancet Haematology. Vol. 5, Issue 1. January 1, 2018. DOI: [https://doi.org/10.1016/S2352-3026\(17\)30232-6](https://doi.org/10.1016/S2352-3026(17)30232-6)

¹ <https://www.cdc.gov/mmwr/volumes/66/wr/mm6636a3.htm>

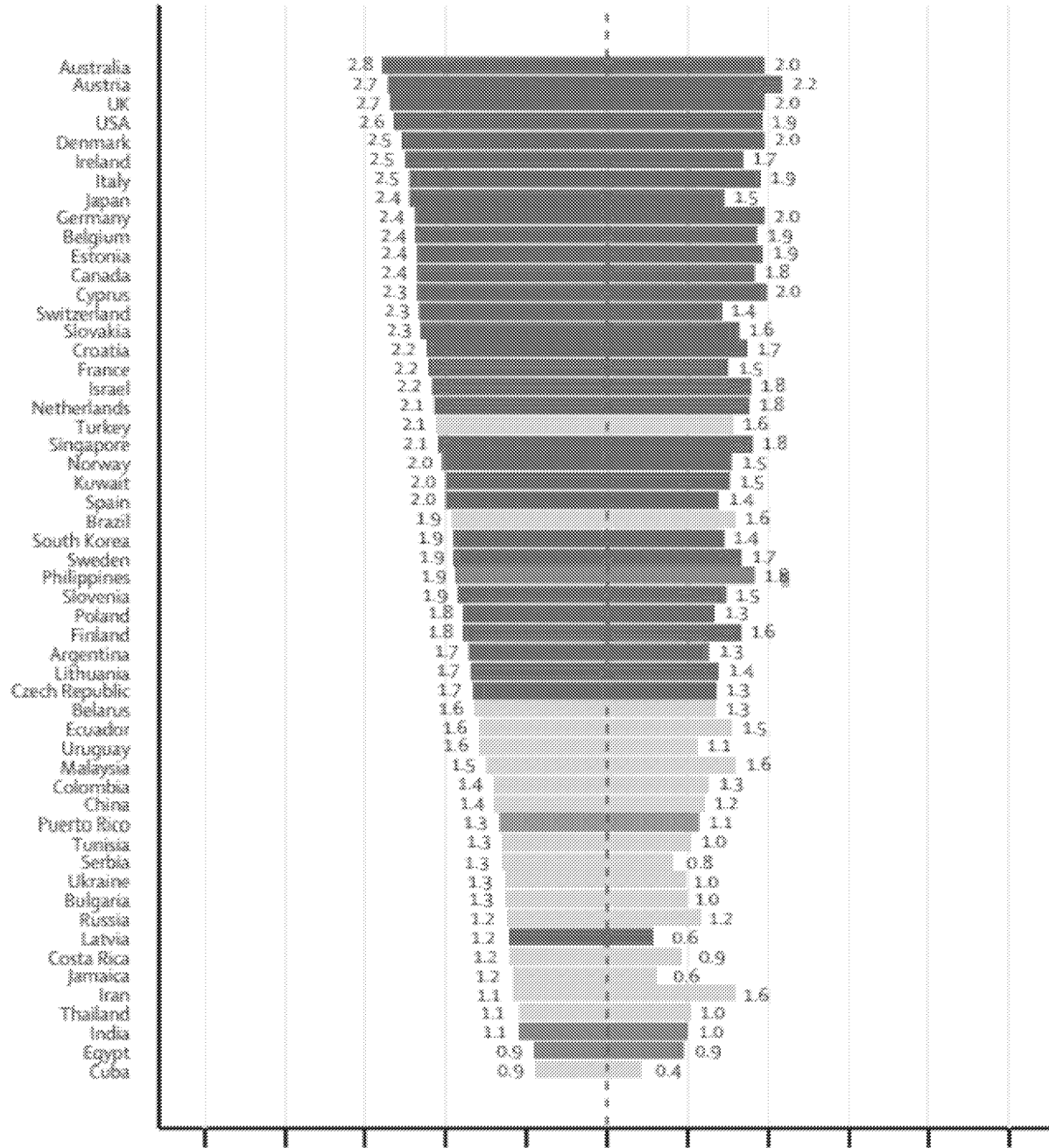
	Cases in men	Age-standardised rates in men (per 100 000)	Cases in women	Age-standardised rates in women (per 100 000)	Male to female ratio
World	200 676	5.6	151 289	3.9	1.4
Africa					
Eastern Africa	4854	3.8	4116	3.4	1.1
Middle Africa	1107	2.6	814	1.8	1.4
Northern Africa	5037	5.6	3731	3.9	1.4
Southern Africa	783	3.6	709	2.6	1.4
Western Africa	1469	1.4	1308	1.2	1.1
America and Caribbean					
Caribbean	1053	4.7	871	3.6	1.3
Central America	4380	5.8	3905	4.9	1.2
South America	10259	5.4	8655	4.1	1.3
Northern America	25 498	10.5	19 464	7.2	1.5
Asia					
Eastern Asia	47 568	5.1	33 986	3.7	1.4
Southeastern Asia	13 826	4.9	11 979	4.0	1.2
South-central Asia	28 870	3.4	19 197	2.3	1.5
Western Asia	7001	6.8	5021	4.8	1.4
Europe					
Central and Eastern Europe	13 170	7.7	11 720	5.1	1.5
Northern Europe	7322	9.2	5200	6.0	1.5
Southern Europe	11 157	8.7	8146	5.6	1.6
Western Europe	14 800	9.6	10 814	6.0	1.6
Oceania					
Australia/New Zealand	2290	11.3	1511	7.2	1.6
Melanesia	199	5.3	130	3.3	1.6
Micronesia/Polynesia	33	5.9	12	2.1	2.9
Data taken from GLOBOCAN, 2012. ¹					
Table: Estimated cases of leukaemia and age-standardised world incidence rates by world region and sex					

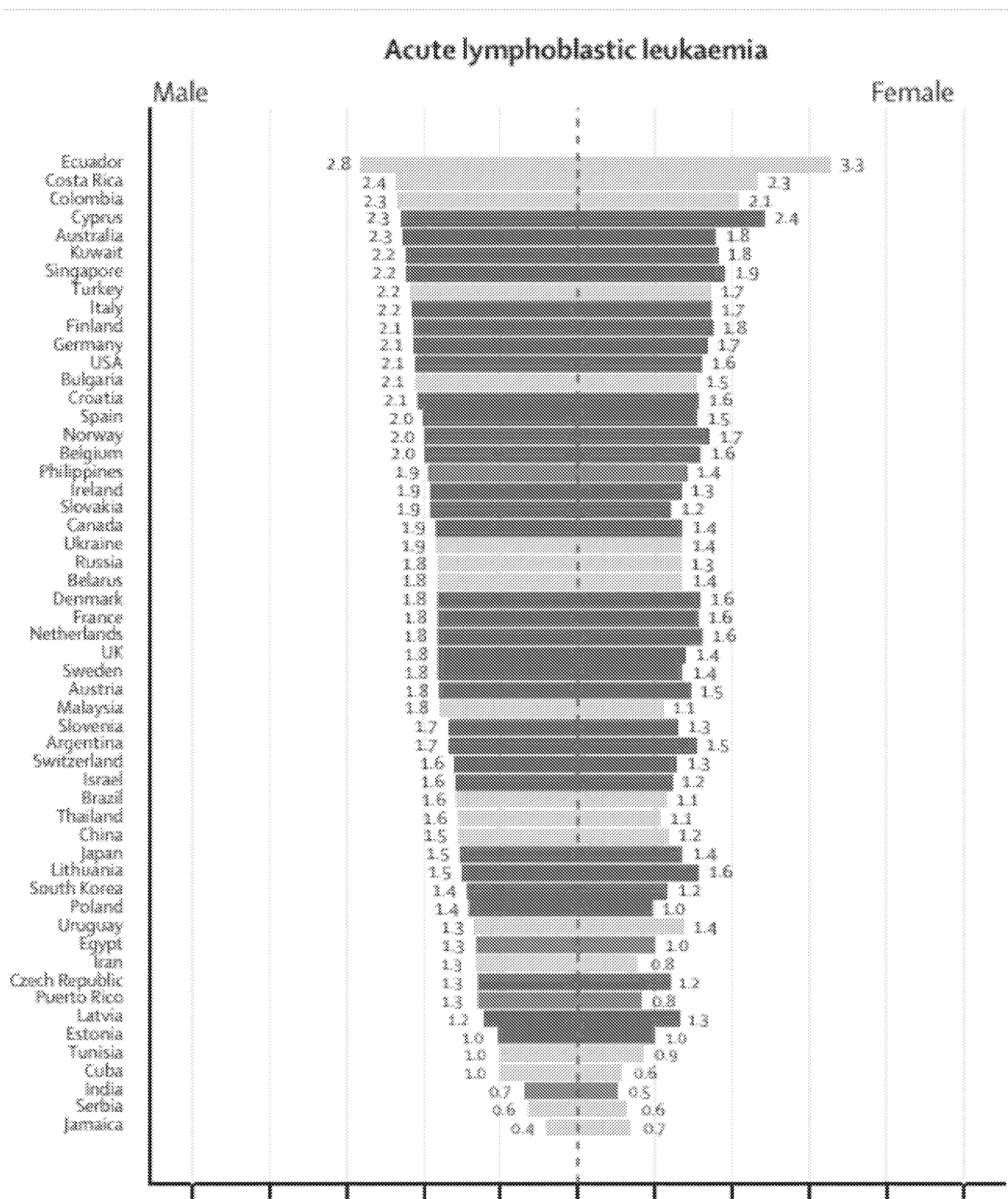
Note that North America collectively accounts for less than 13 percent of cases. Nearly half the cases worldwide are in Asia.

Acute myeloid leukaemia

Male

Female





Per the 2018 Lancet Study, South America has some of the highest rates of acute lymphoblastic leukemia (ALL). The three countries with the highest age adjusted rates of incidence are Ecuador, Costa Rica, and Colombia.

40 USC § 599

At the appropriate time in the licensing process, we expect the National Institutes of Health (NIH) to obtain advice from the Attorney General (as is required under 40 USC § 599) to determine if the “disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law.”

The Bayh-Dole Act provides that “Nothing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law” [35 USC § 211 – Relationship to antitrust laws].

The Bayh-Dole Act sets out the areas where the Bayh-Dole Act “shall take precedence over any other Act which would require a disposition of rights in subject inventions” [35 USC § 210 – Precedence of chapter], and mentions 21 separate statutes, but does not include 40 USC § 599.

The process has lacked transparency

The Federal Register Notice for the license was 550 words. The name of the company (ElevateBio) set to receive the license is mentioned just once. We searched the Internet and could find no web page for ElevateBio. The NIH refused to provide answers to several basic questions about the license (see exchange [here](#)). For example, when asked to identify the key staff, board members or investors of a company with no web page and no Securities and Exchange Commission (SEC) filings, the NIH answered:

“This information is generally publicly available. Any information provided to us that is not publicly available regarding personnel for ElevateBio is considered business confidential information”

The NIH refused to provide information on the federal investments in research and development (R&D) related to the patented invention, explain what measures if any would be used to address access in low and middle income countries, and if the patent term will be for the life of the patent or something shorter.

We have been asking the NIH for data on the costs of the chimeric antigen receptor T-cell (CAR T) trials the NIH has undertaken or funded, and the NIH has resisted providing useful information on that topic.

The key figures in ElevateBio have a record of aggressively pricing drugs

We were able to independently gather some information about the company. According to the Massachusetts business entity registry, ElevateBio is an LLC, first organized in November 2017

in Delaware, and registered in Massachusetts on June 15, 2018. The Massachusetts filing listed four managers: Ansbert Gadicke, David Hallal, Morana Jovan-Embiricos, and Vikas Sinha. Below are a few notes on each of the four managers from the Massachusetts filings.

Ansbert Gadicke

Dr. Ansbert Gadicke co-founded MPM Capital, a healthcare investment firm that invests in companies that develop new therapeutics, particularly for oncology. He was the lead investor and served on the board of BioMarin Pharmaceuticals, Idenix Pharmaceuticals (acquired by Merck & Co.), Radius Health and Mitobridge (acquired by Astellas), and most notably, Pharmasset, which developed the hepatitis C virus (HCV) treatment Sovaldi before being bought by Gilead Sciences for \$11.2 billion.

David Hallal

David Hallal is an executive partner at Dr. Gadicke's MPM Capital. Prior to joining the investment firm, he was CEO of Alexion Pharmaceuticals which developed Soliris, one of the most expensive drugs on the market.² Soliris is classified as an orphan drug, and treats paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). As of May 2017, it was typically priced from \$500,000 to \$700,000 per year.

Morana Jovan-Embiricos

Dr. Morana Jovan-Embiricos previously served as a Partner at MPM Capital, before founding F2 Ventures and F3 Ventures, biotech venture capital funds. She has led and managed a series of biotech investment funds in the US and in Europe. Dr. Jovan-Embiricos, along with Dr. Gadicke, serve as members of the Board of Directors of TCR2 Therapeutics, an immuno-oncology company that focuses on T cell receptor-based cellular therapies.

Vikas Sinha

Vikas Sinha is also an executive partner at MPM Capital, and previously worked alongside David Hallal, as CFO at Alexion Pharmaceuticals. He has also served in many roles at Bayer, including as Vice President and CFO of Bayer Pharmaceuticals in the US, and Vice President and CFO of Bayer Yakuhin in Japan.

Considering the background of ElevateBio's founders, the NIH can expect the price for the new CAR T treatment to be aggressive, unless the NIH includes provisions in the license to restrain the prices.

2

<https://www.bloomberg.com/news/features/2017-05-24/when-the-patient-is-a-gold-mine-the-trouble-with-rare-disease-drugs>

Low- and middle-income countries

We ask that the NIH limit the exclusivity in the license to countries that have per capita incomes that are at least 30 percent of the United States, and to provide a public and transparent set of commitments to ensure that the therapy is available broadly in countries that are low- and middle-income.

We support this request with the following comment.

According to the “United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy:”

“PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries.”

Designated Countries

The NIH should further clarify the geographic area of the license. We note that according to the WIPO PatentScope web page, the designated countries for PCT/US2017/034691 (the International Patent Application listed in the notice) are as follows:

Designated States: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

African Regional Intellectual Property Organization (ARIPO) (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW)

Eurasian Patent Office (AM, AZ, BY, KG, KZ, RU, TJ, TM)

European Patent Office (EPO) (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR)

African Intellectual Property Organization (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)

This includes most of sub-Saharan Africa as well as many countries of middle- and low-income status in other regions. If the policy of the NIH is to withhold patents or exclusive rights in countries with low and middle incomes, it needs to address that in the license itself, and not permit patent filings in all of the currently PCT-designated countries.

MPP

We ask the NIH to reach out to the Medicines Patent Pool (MPP), in order to enter into an agreement that gives the MPP an option to negotiate non-exclusive open licenses for the inventions in developing countries. We note the MPP has recently expanded its mandate to treatments for cancer and other disease.

Definitions of countries with access challenges

We also ask the PHS to reconsider the use of the term “developing countries,” which is no longer the most useful way to describe a category of countries for which access is a challenge.

There is no consensus on how to define “developing countries.” The WTO allows its members to self-identify as “developing.”

Policy makers often prefer to use the term “low- and middle-income countries” (LMIC), but this also requires a thoughtful definition.

The World Bank publishes and updates a list of country classifications every year, but the World Bank definition is anchored in a methodology from the 1980s that was based in part upon the cost of buying food, a poor proxy for global wellbeing today.

The World Bank definition of “high income” was adopted in 1989 by the Bank’s Executive Directors on the basis of a staff report on per capita income measures. The high income threshold was determined by an “explicit benchmark of \$6,000 per capita in 1987 prices,” and updated annually with an adjustment for inflation. With real growth in per capita incomes, the number of countries that qualify as high income has continued to rise, and at some point, most countries will probably qualify.

Our recommendation is that the NIH consider relative per capita income as a useful starting metric for policies designed to mitigate inequality of access, recognizing that in some cases other factors such as prevalence of a disease may be appropriate to consider. As noted above, 30 percent of U.S. per capita income is a good starting point for identifying countries with significant challenges in regard to access.

35 USC § 209

Assuming the NIH has conducted a proper analysis to determine if any exclusive rights are necessary to induce investments in R&D to bring the inventions to practical application, we ask the NIH to limit the “proposed scope of exclusivity” so that it is “not greater than reasonably necessary to provide the incentive for bringing the invention to practical application,” as is required by 35 USC § 209.

Such an analysis should include an estimate of the expected costs (adjusted for risks and the costs of capital) to bring the invention to practical application, as well as reasonable estimates of the revenue from the sale of the technology that would be necessary as an adequate incentive for that investment. If the expected investments are small (which seems to be the case given the modest size of the clinical trials for other CAR T therapies) then the NIH should limit either (1) the number of years of exclusivity, (2) the prices that can be charged, (3) the maximum revenue earned before exclusivity is reduced or eliminated, or (4) some combination of 1-3.

35 USC § 201(f) – definition of practical application

The Bayh-Dole Act defines certain terms in 35 USC § 201, including the term “practical application.”

(f) The term “practical application” means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms. [emphasis added]

“Available to the public” and “reasonable terms” taken together include the price to the public being reasonable. For the public, the price is the primary term of the transaction.

Proposals for safeguards to protect the public’s rights in the patented inventions

We propose the following measures to protect the public’s interest in any license to ElevateBio.

No discrimination against U.S. residents in pricing

We ask that the NIH include language in the proposed exclusive license to ensure that the prices in the U.S. for any health technology using the inventions are not higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

We consider this a modest and indeed minimalist request to protect U.S. residents, who paid for the R&D that created the licensed inventions.

We further note that President Donald Trump and Secretary Alex Azar have made recent comments in support of policies to impose international reference pricing for certain Medicare Part B drugs in some geographic areas, justified in part by the goal of reducing discrimination against U.S. residents. In this case, when the R&D for a treatment is subsidized by U.S. taxpayers, the rationale for including a non-discrimination provision is even stronger.

Additional provisions on affordability

The NIH should require that prices for products in the United States that use NIH-owned patented inventions do not exceed the estimated value of the treatment, as determined by independent health technology assessments selected by HHS.

The NIH should also create an obligation to set prices low enough that patient co-payments under third party Medicare programs are affordable.

Reduce term of exclusivity when revenues are large

In addition to an external reference pricing test, we propose that the exclusivity of the license in the U.S. should be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks.

Given the modest cost of acquiring an NIH-patented invention, the amount of money the developer needs in sales to justify additional investments in R&D is reduced, as compared to cases where a company develops or acquires the technology from non government sources.

This request is consistent with the statutory requirements of 35 USC § 209, which demands that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”

One possible implementation of revenue benchmarks is as follows: exclusivity will be reduced by one year for every \$500 million in revenue equivalents, earned after the first \$1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. However, the NIH could choose different benchmarks, including even lower benchmarks, if the data on R&D costs will support a lower threshold, so long as the limits on exclusivity address the requirements of 35 USC § 209, in that the incentive is “not greater than reasonably necessary.”

Test data

In addition, we ask the NIH to include provisions that would require the licensed patent holders to waive any exclusive rights regarding test data that may exist in any country with a per capita income less than 30 percent of U.S. per capita income. This is important because a number of trade agreements and bilateral pressures force low and middle income countries to enact laws granting exclusive rights in test data, in most cases, without the possibility of exceptions, even in cases involving excessive prices.

A provision waiving exclusive rights in test data in countries with lower incomes is necessary for the NIH to implement the PHS policy “to promote commercial development of inventions in a way that provides broad accessibility for developing countries.”

Transparency

The licensee should be required to file an annual report to the NIH on the research and development costs associated with the development of any product that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 USC § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

Sincerely,

Organizations

Health GAP

Knowledge Ecology International (KEI)

Public Citizen

Social Security Works (SSW)

Union for Affordable Cancer Treatment (UACT)

Individuals

James Love

Ophira Ginsburg, MD

From: Joe Allen [jallen@allen-assoc.com]
Sent: 5/13/2019 8:49:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Re: Ashley

The Committee's trying to decide between Ashley and Stephen Ezell from ITIF (who I recommended earlier). Told them that Ashley might be the stronger witness, as he's more likely to be able to rebut misleading data on specific drug development cases in real time, but either one would do a good job.

Feel better that someone from our side of the debate should be there.

By the way, did you see Fred Reinhart's piece "KEI's misleading letter to Congress on March in Rights" in today's IP Watchdog?

Jamie Love wrote asking to write a rebuttal, which the editor said is fine.

Should be an interesting week!

On 5/13/2019 3:24 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

yeah

From: Joe Allen <jallen@allen-assoc.com>
Sent: Monday, May 13, 2019 3:11 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Re: Ashley

He said he'd do it!

Sent from my iPhone

On May 13, 2019, at 2:50 PM, Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov> wrote:

Ashley Stevens
Focus IP Group, LLC
Winchester, MA

Office: (781) 721-2670
Cell: b6

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Office of Science Policy
National Institutes of Health

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719

REL0000024515

(W) 740-484-1814

(c) b6

www.allen-assoc.com

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 11/29/2018 8:20:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]
Subject: KEI litigation question

Mark—

b5

b5

Thanks, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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REL0000024519

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/20/2018 6:31:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Rydapt - failure to disclose federal funding

From: Andrew Goldman <andrew.goldman@keionline.org>
Sent: Tuesday, March 20, 2018 1:22 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>
Subject: Rydapt - failure to disclose federal funding

Dear Dir. Hammersla:

I wanted to provide you a courtesy notice that we are finalizing a document similar to the two we have sent in recent days, this time requesting that NIH conduct an investigation into the failure to disclose federal funding leading to the expensive medicine Rydapt (INN midostaurin). The document requests that NIH remedy that failure by taking title to the patents at issue. The memorandum and appendices will detail the grants issued to inventor James Griffin, and their relationship to the patents.

Kind regards,

Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

REL0000024523

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 10/30/2017 4:43:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Petrik, Amy (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c4ec05a179f04067b61f20605e911e7c-petrika]; Salata, Carol (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98ca6a1f9fc4cfdbbf4036ca8cbace4-csalata]; Felicia, Vincent (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7f3a54860cb941c1abe1df786e478e00-vfelicia]; Green, Wade (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=88fdd3b0456c40458e952e6c043b2a6b-williamswa]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]; Sayyid, Fatima (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b9e45041bdb43719f7113a5aae27057-sayyidf]
Subject: Re: ACTION DUE 5 PM TODAY, 30 Oct 2017- Responses to FRN

Thanks Mark. I'll get a read from NIAID comms before Amy responds.

On Oct 30, 2017, at 12:31 PM, Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov> wrote:

I agree but do you want [REDACTED] b5
[REDACTED] b5
I'm thinking [REDACTED] b5
[REDACTED] b5

Sent from my iPhone

On Oct 30, 2017, at 12:20 PM, Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov> wrote:

Thanks very much for your prompt reply!

Mark - [REDACTED] b5
[REDACTED] b5
[REDACTED] b5

Including Fatima here for here awareness.

Thanks,

Mike

On Oct 30, 2017, at 11:49 AM, Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov> wrote:

Hi Mike,

I've received one response to date in the form of an email on Wednesday, Oct. 25 from Kim Treanor of KEI.

REL0000024524

She enquired about whether NIH has provided or intends to provide any financial support to PaxVax for clinical trials of the subject vaccine candidate. Additionally, she cited the PaxVax-CDC CRADA on Zika vaccine development and asked if any funding has been provided for that vaccine.

I'll update you all if I receive and further communications from the FRN.

Please let me know if you have any questions.

Best,
Amy

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Monday, October 30, 2017 11:36 AM
To: Petrik, Amy (NIH/NIAID) [E] <amy.petrik@nih.gov>; Salata, Carol (NIH/NIAID) [E] <csalata@niaid.nih.gov>
Cc: Feliccia, Vincent (NIH/NIAID) [E] <vfeliccia@niaid.nih.gov>; Green, Wade (NIH/NIAID) [E] <wade.green@nih.gov>; Frisbie, Suzanne (NIH/NIAID) [E] <suzanne.frisbie@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: ACTION DUE 5 PM TODAY, 30 Oct 2017- Responses to FRN

Hi Amy & Carol,

I'm curious about the status of the FRN.

Please reply to all recipients of this message to confirm:

- Whether you have received any responses to the Zika FRN
- If so, from what organization/s

Thanks!

Mike
Michael R. Mowatt, Ph.D.
Director, Technology Transfer and Intellectual Property Office

National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services

+1 301 496 2644

<image001.jpg>

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From: Fine, Amanda (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=61290B74AA9A44358954C45439FFDEB6-FINEAB]
Sent: 8/8/2017 7:49:45 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertsond]
CC: Burke, Andy (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=305e280edc664e68939d4348603f56e6-burkear]; Myles, Renate (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7d317f5626934585b3692a1823c1b522-mylesr]; Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]; Hatch, Shannon (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=562f6d8791de4aa1837656c095c280a2-hatchsp]
Subject: RE: TIMELY HuffPost request

Thanks Mark! I'm also looping in Dave who I understand is point on this. I've included the proposed revised language below:

b5

Thanks again to all for the help,
Amanda

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, August 08, 2017 3:48 PM
To: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>
Cc: Burke, Andy (NIH/NCI) [E] <burkear@mail.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Hatch, Shannon (NIH/NCI) [E] <hatchsp@mail.nih.gov>
Subject: Re: TIMELY HuffPost request

I would [b5] As a general response, what you provided works but I would suggest editing to say [b5]
[b5] Thx

Sent from my iPhone

On Aug 8, 2017, at 3:16 PM, Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov> wrote:

Hello-

Just following up on my email from earlier. I know it's a tight turnaround and Mark is out, but Andy perhaps you are able to weigh in?

REL0000024525

Thanks!
Amanda

From: Fine, Amanda (NIH/OD) [E]
Sent: Tuesday, August 08, 2017 12:36 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hardesty, Rebecca (NIH/OD) [C] <rebecca.hardesty@nih.gov>; McBurney, Margaret (NIH/OD) [E] <mmcburney@od.nih.gov>; Burke, Andy (NIH/NCI) [E] <burkear@mail.nih.gov>
Cc: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>; Hatch, Shannon (NIH/NCI) [E] <hatchsp@mail.nih.gov>
Subject: FW: TIMELY HuffPost request

Greetings-

We received the below inquiry about the prospective grant of exclusive license to Salubris as a result of another KEI letter. The reporter's deadline is as soon as possible. We are hoping you are able to help us in drafting a response. Below is language we've used in the past on this topic that may be applicable or a good starting point:

b5

Please let me know if you have any questions or concerns.

Thank you in advance for your guidance,
Amanda

Amanda Fine
Deputy, News Media Branch
National Institutes of Health
Tel: 301-496-7246
Email: amanda.fine@nih.gov
Web: <http://www.nih.gov>

NIH . . . Turning Discovery Into Health

From: Alexander Kaufman [<mailto:alexander.kaufman@huffpost.com>]
Sent: Tuesday, August 08, 2017 12:12 PM
To: Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: TIMELY HuffPost request

Hello,

I left a voicemail earlier, but wanted to follow up here. I am writing a story on the exclusive license NIH proposed giving to

REL0000024525

Salubris: <https://www.federalregister.gov/documents/2017/08/07/2017-16525/prospective-grant-of-exclusive-patent-license-the-development-of-a-bispecific-biparatopic>

I know Jamie Love from Knowledge Ecology International submitted a letter to David Lambertson this morning. I also emailed David. But I wanted to reach out to give NIH a chance to comment. I'm available at b6

--

Alexander C. Kaufman

Business & Environment Reporter

<image002.jpg>

o: 917-606-4668

m: b6

@AlexCKaufman

From: Knabb, Jim (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=535517D229E04963A2B928742CB80DA0-KNABBJR]
Sent: 11/29/2018 8:46:47 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: RE: Response to comments from KEI for A-548-2018
Attachments: A-548-2018_Response to KEI.pdf

Thank you Mark,

The comments from you and Dale are greatly appreciated. Richard and I discussed this and I'm going to reply to KEI's comments with the attached pdf.

Thanks again,
Jim

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, November 29, 2018 11:51 AM
To: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: RE: Response to comments from KEI for A-548-2018

Jim:

Thanks for sending this over. Dale and I have provided comments in the attached.

Let me know if you have further questions.

Mark

From: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>
Sent: Wednesday, November 28, 2018 4:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: Response to comments from KEI for A-548-2018

Mark,

I received questions from James Love at KEI in response to an Intent to Grant (NIH reference A-548-2018 ([link](#))).

We wanted to submit these answers to you prior to responding to KEI in an effort to maintain consistency in the NIH's response to FRN comments. The questions and responses can be found in the attached word document and I'd be happy to discuss as you see necessary.

Many thanks,
Jim

Jim Knabb, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center

REL0000024526

9609 Medical Center Drive, RM 1E530 MSC 9702
Bethesda, MD 20892-9702 (for USPS mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Direct line: (240) 276-7856
knabbir@mail.nih.gov



29 November 2018

VIA E-MAIL ONLY

James Love
Knowledge Ecology International
1621 Connecticut Ave. NW, Suite 500
Washington, DC 20009

IN RE: Prospective Grant of an Exclusive License (NIH License Application A-548-2018) to ElevateBio,
published on 19 November 2018 in *Federal Register* Vol. 83, No. 223, page 58262

Dear Mr. Love:

Thank you for submitting questions regarding the notice of the proposed license to ElevateBio by the National Cancer Institute (NCI). Please find responses to these questions where available below (responses in **bold**):

1. Does ElevateBio have a web page?

- **Generally, the existence of web pages is publicly available and information that can be ascertained by the commenting party using any number of internet search engines.**

2. Does ElevateBio have any SEC filings?

- **Similar to Question 1 above, a search for SEC filings can be performed by the commenting party via the SEC website.**

3. Are any of the key staff, board members or investors current or former NIH employees?

- **NIH ethics regulations would generally prohibit current employees or recently departed employees from participating in such roles.**

4. Who are the key staff, board members or investors?

- **This information is generally publicly available. Any information provided to us that is not publicly available regarding personnel for ElevateBio is considered business confidential information**

5. Is there any public evidence to evaluate the capacity of ElevateBio to financing the development of this technology?

- **As required by 37 CFR 404, the evidence necessary to evaluate the capacity of ElevateBio to develop this invention was contained within the license application, which is considered business confidential information.**

6. What is the status of or intentions for national filings for the following countries listed on the WIPO PCT page?

- **The status of the intellectual property associated with the technology for which a license is proposed is accurately provided in the Notice of Intent to Grant.**

7. According to the United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy:



“PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries.”

What concrete measures will the NIH include to implement this objective?

- We do not anticipate filing patent applications in developing countries, which will permit the invention to be exploited in those jurisdictions. We anticipate that the exclusive grant of rights to ElevateBio will make possible the commercial development of a product that can be used by patients throughout the world.

8. What is the status of the development of this technology? Specifically, what trials if any has the NIH funded or undertaken relating to this technology/treatment?

- The technology is at an early stage of preclinical development, and requires partnering with industry to ensure that clinical trials can be conducted on a scale necessary to support FDA approval.

9. How much money has the NIH spent on research directly related to the technology to be licensed?

- NCI's Technology Transfer Center does not have access to the budgets and costs of individual labs/projects as it is not our purview to monitor research expenses.

10. Will the license be life of patent or less than life of patent?

- The terms of the agreement have not yet been negotiated.

11. What concrete measures will the NIH include in the license to ensure that the inventions are "available to the public on reasonable terms", which is a requirement of the Bayh-Dole Act?

- Such measures are yet to be negotiated. Our licenses typically include benchmarks designed to perfect and develop the invention, clinically test it, and make it as widely available as possible to advance public health.

If I can be of any further assistance, please let me know.

Sincerely,
Jim Knabb, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute, TTC
Jim.Knabb@nih.gov

From: Wong, Jennifer (NIH/NIMH) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=C4258C7CF58F4945A3DF079942C68852-WONGJE]
Sent: 5/6/2019 7:41:10 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: FR Notice

Hi Mark,

Thanks for the heads-up. Of course, I'll draft a response and forward it to you for comment.

Thanks for your help!
Jenny

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, May 6, 2019 9:55 AM
To: Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov>
Subject: Re: FR Notice

And by the way, I will have a AAAS fellow working with me starting in the fall. Her name is Jennifer Wong. I will call you Jenny and her Jennifer but if you get what seems like a strange email from me, it is probably for her.

Sent from my iPhone

On May 6, 2019, at 9:30 AM, Wong, Jennifer (NIH/NIMH) [E] <jennifer.wong2@nih.gov> wrote:

Hi Mark,

To keep you in the loop: KEI had some questions about NIMH's recent FR Notice. If you would like to discuss, please let me know.

Best,
Jenny

Jennifer Wong, M.S.
Technology Development Coordinator
National Institute of Mental Health
Office of Technology Transfer
35A Convent Drive, Room GE400
Bethesda, MD 20892-3747
Phone: 301-480-4821
E-mail: wongje@mail.nih.gov

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From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 10/17/2016 6:59:59 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Meeting with Emily

Hello Mark: I just sent a meeting request so that we can meet with Emily to learn what she has been saying to KEI, etc. Dale responded that he could not meet. I am thinking we can go ahead with this background meeting that appears Emily has already briefed him on. Thoughts?

Ann

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Dodson, Sara (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=985A956EAA0D4945BDCFD8EA30947D68-DODSONSE]
Sent: 7/20/2018 2:38:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Gadbois, Ellen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0243d1d6e6f248268d2edec566c26c2a-gadboisel]
Subject: RE: CONFIDENTIAL list of attendees for Harvard meeting

Interesting. I know [b6] She's another one of the [b6] a couple of years ago. She studies the economics of drug development and innovation. I've never heard her discuss March-in but I'd be surprised if she were a proponent.

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 5:39 PM
To: Dodson, Sara (NIH/NIAID) [E] <sara.dodson@nih.gov>; Gadbois, Ellen (NIH/OD) [E] <gadboisel@od.nih.gov>
Subject: CONFIDENTIAL list of attendees for Harvard meeting

I was invited to this closed meeting in Dec about " of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution."

[b6] has been active writing for years about use of march-in to reduce prices. [b6] you probably know. We know [b6] [b6] are in the same camp. Of course we know [b6] (odd that he would be coming). Do you know any of the others and their general positions on issues like this?

-----Original Message-----

From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Thursday, July 19, 2018 5:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

We hope so. The (at this point, confidential) list of other invitees is below. We would welcome your participation as a member of the conversation throughout the meeting, or for a half-day period, or even as a guest speaker at lunch or dinner. We will operate under 'Chatham House Rules' such that there will be no quotes attributed to anyone.

Let me know what you think! We believe it will be very useful to have your perspective and contribution-

Best,
Aaron

b6

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Thursday, July 19, 2018 5:05 PM
To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

REL0000024529

Aaron:

I am considering your invitation to the Dec meeting. Will the attendees represent a breadth of thinking and opinions about this issue?

Thanks
Mark

-----Original Message-----

From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 4:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

So noted! This is all for our background knowledge. Thanks for responding!

Any initial thoughts about joining us in Boston for the December event?

ASK

-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 4:03 PM
To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Aaron:

Note that I do not give permission to publish or otherwise publicize my direct comments without permission.

By the late 1980s, NIH was using one standard model agreement for all types of CRADA collaborations. We noted later that some types of collaborations required fewer terms in this standard agreement. In particular, when the collaboration involved primarily the receipt and training in the use of unique research materials from a company, terms dealing with other matters such as human subjects, reports from the company, regular meetings between the parties, etc. were not relevant and therefore not needed. Rather than send a company lawyer a document with a number of nonrelevant terms to be deleted, NIH developed a M-CRADA stripped down to the terms relevant to or otherwise legally required in a collaboration involving primarily materials. It sped up negotiation and thus benefited both the NIH and the company providing the unique materials.

Since then other CRADA models were developed to suit particular types of commercial collaborations, e.g. clinical research.

CRADA partners do not decide on which model, NIH decides.

-----Original Message-----

From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 11:21 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

Thanks Mark! This is very useful--I will read this over. Here are the questions we have, which may not be covered by this overview:

1. What's the difference between a CRADA and a Materials CRADA (MCRADA)? In particular, are there any cost benefits or differences in accessibility between a CRADA and an MCRADA?
2. Prior to 1996 (when the NIH initiated MCRADAs), could any of the signed CRADAs cover what is now included in an MCRADA?
3. How do potential CRADA partners decide between a CRADA and a MCRADA?
4. What motivated the NIH to introduce the MCRADA mechanism in 1996?

Let me know if this is worth a phone call.

On a different note, we're organizing a Radcliffe Seminar at Harvard this winter (December 11-12) on the subject of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution. It's a small group session of like 15 or so experts in science, economics, law, and medicine from around the country. It would be great to have you join us if not for the whole time, at least as a guest/featured speaker over lunch or dinner -- would something like that be possible?

Best,
Aaron

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-----Original Message-----

From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 11:16 AM
To: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Here is NIH's overview of CRADAs. <https://www.ott.nih.gov/policy/cradas>

-----Original Message-----

From: Kesselheim, Aaron Seth, M.D., M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Tuesday, July 17, 2018 10:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Questions about CRADAs

Hi Mark -- hope all is well. One of the people in my research group is doing a project on CRADAs and had a few fundamental questions that I thought you might be able to help with -- would it be ok to send the questions over email, or maybe set up a time to quickly chat?

Best,
Aaron

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Associate Professor of Medicine at Harvard Medical School Director, Program On Regulation, Therapeutics, And Law (PORTAL) Division of Pharmacoepidemiology and Pharmacoeconomics Brigham and Women's Hospital
1620 Tremont St, Suite 3030
Boston MA 02120
akesselheim@partners.org
P: 617-278-0930; F: 617-232-8602
<http://www.PORTALresearch.org>

Faculty member, Harvard Medical School Center for Bioethics Irving S. Ribicoff Visiting Associate Professor of Law, Yale Law School (2016-2018) Editor-in-Chief, Journal of Law, Medicine, and Ethics

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REL0000024529

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/20/2018 7:27:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Cooper, Scott (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4655dfd7c5cf414ea19d3f3be423f088-coopersa2]; Deutsch, Mary Frances (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1dfd60551fcc40ff8ca4caa248f73d94-deutschm]
Subject: FW: Rydapt - failure to disclose federal funding

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, March 20, 2018 3:27 PM
To: 'Andrew Goldman' <andrew.goldman@keionline.org>
Cc: Jamie Love <james.love@keionline.org>; Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>
Subject: RE: Rydapt - failure to disclose federal funding

Dear Andrew:

Thank you for your courtesy notice that KEI is submitting a new request asking the NIH to take ownership actions for Rydapt.

NIH will review the Rydapt request and NIH's funding, if any, and is now reviewing the earlier requests you have submitted and will you and KEI know the results of NIH's internal research.

Ann

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Andrew Goldman <andrew.goldman@keionline.org>
Sent: Tuesday, March 20, 2018 1:22 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Jamie Love <james.love@keionline.org>
Subject: Rydapt - failure to disclose federal funding

Dear Dir. Hammersla:

I wanted to provide you a courtesy notice that we are finalizing a document similar to the two we have sent in recent days, this time requesting that NIH conduct an investigation into the failure to disclose federal funding leading to the expensive medicine Rydapt (INN midostaurin). The document requests that NIH remedy that failure by taking title to the

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patents at issue. The memorandum and appendices will detail the grants issued to inventor James Griffin, and their relationship to the patents.

Kind regards,

Andrew S. Goldman
Counsel, Policy and Legal Affairs
Knowledge Ecology International
andrew.goldman@keionline.org // www.twitter.com/ASG_KEI
tel.: +1.202.332.2670
www.keionline.org

From: Girards, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=6F43C30C4A364463BF5B2C134225B7F0-GIRARDSRT]
Sent: 10/25/2017 9:18:13 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: paper and blog of interest
Attachments: Capstone Project submission as of 25 Oct 2017.docx

Dear Mark-

Attached is a draft- thanks again for agreeing to be a mentor on this project!

Please do let me know if you have any questions or comments. I have discussed a prior draft with Steve Ferguson and incorporated his comments into the attached draft.

In terms of timing, I'll have to submit a final work product about the first week of December- I've budgeted the month of November for you and me to update (if necessary) this draft.

-Rick

Richard T. Girards, Jr., Esq., MBA
National Institutes of Health
NCI Technology Transfer Center
9609 Medical Center Drive, Room 1E508 MSC 9702
Rockville, MD 20850-9702 *for UPS/FedEx/visitors*
Bethesda, MD 20892-9702 *for U.S. Mail*
richard.girards@nih.gov
Phone: 240-276-6825
Fax: 240-276-5504
<http://ttc.nci.nih.gov>

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, September 29, 2017 11:09 AM
To: Girards, Richard (NIH/NCI) [E] <richard.girards@nih.gov>
Subject: RE: paper and blog of interest

Looks good. A few suggestions. Also please be careful to make clear that this is done as part of your outside activity not official work activity. Employees cannot advocate for legislation, and these are your personal ideas not those of NIH or NCI. That is not to say they would not be useful to NIH, just not official work product.

From: Girards, Richard (NIH/NCI) [E]
Sent: Friday, September 29, 2017 9:44 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: paper and blog of interest

Dear Mark-

Any thoughts as to the below?

Thanks.

REL0000024531

-Rick

From: Girards, Richard (NIH/NCI) [E]
Sent: Monday, September 25, 2017 9:25 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: paper and blog of interest

Thanks again, Mark- I greatly appreciate it.

In terms of a defined "mission/deliverables statement" for my capstone project, I have formulated the following:

b6

Would this type of work product be useful to your office ... in addition, do you have any comments as to the proposed scope?

-Rick

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, September 21, 2017 12:26 PM
To: Girards, Richard (NIH/NCI) [E] <richard.girards@nih.gov>
Subject: paper and blog of interest

Rick:

Here is a link to the CellPro march-in I mentioned. <http://scholarship.law.berkeley.edu/btlj/vol14/iss3/7/>

Interesting new blog about research impact. I was thinking about it in terms of some of the discussion near the end as to how we communicate with greater society about impacts of what we are doing. How do we communicate with the public about these issues of the role of NIH. Just a thought. <http://www.sciencemetrics.org/research-impact-now/>

Mark
Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

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From: Stevens, Ashley J [astevens@bu.edu]
Sent: 4/14/2017 11:33:20 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Re: Could you please send me your KEI comments

Traveling to [b6] I'll send them as soon as I get to the hotel, maybe 3 hours.

Sent from my iPhone -- please excuse typo's

Ashley J Stevens
Focus IP Group LLC
Winchester, MA 01890
USA
Phone: (781) 721-2670
Cell: [b6]
Email: astevens@bu.edu

> On Apr 14, 2017, at 2:53 PM, Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@od.nih.gov> wrote:
>
> Ashley:
>
> I am on travel and my supervisor would find helpful your KEI talking points for internal use. Could
you send them to me please this morning.
>
> Thanks much
> Mark
>
> Sent from my iPhone

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 11/29/2018 4:24:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Response to comments from KEI for A-548-2018
Attachments: A-548-2018_Response to KEI--OGCBerkleyComments.docx

Thanks. Here are my suggestions

b5

b5

b5

I'll let you forward this to Jim if ok with you.

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, November 28, 2018 4:57 PM
To: Berkley, Dale (NIH/OD) [E] <berkeleyd@od.nih.gov>
Subject: FW: Response to comments from KEI for A-548-2018

Dale:

See attachment. I have concerns about

b5

b5

Thx

From: Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov>
Sent: Wednesday, November 28, 2018 4:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>
Subject: Response to comments from KEI for A-548-2018

Mark,

I received questions from James Love at KEI in response to an Intent to Grant (NIH reference A-548-2018 ([link](#))).

We wanted to submit these answers to you prior to responding to KEI in an effort to maintain consistency in the NIH's response to FRN comments. The questions and responses can be found in the attached word document and I'd be happy to discuss as you see necessary.

Many thanks,
Jim

Jim Knabb, Ph.D.

REL0000024533

Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Drive, RM 1E530 MSC 9702
Bethesda, MD 20892-9702 (for USPS mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Direct line: (240) 276-7856
knabbir@mail.nih.gov

b5

b5

From: Garcia-Malene, Gorka (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=4C4DA0F5E0A0480AAD2A86924CABA7B7-GARCIAMALEN]
Sent: 10/19/2017 5:01:51 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: FOIA requests on exclusive licensing

Thank you for that background.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, October 19, 2017 12:30 PM
To: Garcia-Malene, Gorka (NIH/OD) [E] <gorka.garcia-malene@nih.gov>
Subject: RE: FOIA requests on exclusive licensing

Prior to 2006, James Love was President of "Essential Inventions." Not sure if they filed FOIAs back then.

From: Garcia-Malene, Gorka (NIH/OD) [E]
Sent: Thursday, October 19, 2017 9:37 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: FOIA requests on exclusive licensing

I'm in room 5B31B.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 5:40 PM
To: Garcia-Malene, Gorka (NIH/OD) [E] <gorka.garcia-malene@nih.gov>
Subject: RE: FOIA requests on exclusive licensing

I will come by at 11:30. What room?

From: Garcia-Malene, Gorka (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 5:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: FOIA requests on exclusive licensing

Any time before 1 pm should work well. I look forward to it!

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 5:30 PM
To: Garcia-Malene, Gorka (NIH/OD) [E] <gorka.garcia-malene@nih.gov>
Subject: RE: FOIA requests on exclusive licensing

Yes. I could come by any time after 11 tomorrow if that works.

From: Garcia-Malene, Gorka (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 5:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: FOIA requests on exclusive licensing

Yes, in 31. Is that nearby?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 5:25 PM
To: Garcia-Malene, Gorka (NIH/OD) [E] <gorka.garcia-malene@nih.gov>
Subject: RE: FOIA requests on exclusive licensing

Certainly. Welcome!!
I am Bldg 1, are you on campus?

From: Garcia-Malene, Gorka (NIH/OD) [E]
Sent: Wednesday, October 18, 2017 4:33 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FOIA requests on exclusive licensing

Good afternoon,

My name is Gorka Garcia-Malene. I joined NIH this week to serve as the agency's FOIA Officer. I am in the process of being briefed on internal processes, caseloads, deadlines, and the like. Looking over the pending FOIAs, we have identified a few that deal with exclusive licensing. I believe that a few responsive records were sent our way from your office. I wonder whether we might make some time to introduce ourselves and discuss these requests.

Kind regards.

Gorka

From: Knabb, Jim (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=535517D229E04963A2B928742CB80DA0-KNABBJR]
Sent: 11/28/2018 9:23:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: Response to comments from KEI for A-548-2018
Attachments: A-548-2018_Response to KEI.docx

Mark,

I received questions from James Love at KEI in response to an Intent to Grant (NIH reference A-548-2018 ([link](#))).

We wanted to submit these answers to you prior to responding to KEI in an effort to maintain consistency in the NIH's response to FRN comments. The questions and responses can be found in the attached word document and I'd be happy to discuss as you see necessary.

Many thanks,
Jim

Jim Knabb, Ph.D.
Senior Technology Transfer Manager
NCI Technology Transfer Center
9609 Medical Center Drive, RM 1E530 MSC 9702
Bethesda, MD 20892-9702 (for USPS mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Direct line: (240) 276-7856
knabbir@mail.nih.gov

b5

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 4/26/2019 5:22:35 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: NIH march-ins

Most of the open cases were delegated but there are 1-2 that came directly to NIH through the Director.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, April 26, 2019 1:21 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: NIH march-ins

The report says 12 to NIH. b5

From: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Sent: Friday, April 26, 2019 12:08 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: NIH march-ins

Yes - only counting the march-ins at NIH.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, April 26, 2019 12:06 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: NIH march-ins

Those are at HHS right? b5

Sent from my iPhone

On Apr 26, 2019, at 12:01 PM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

I believe they are the ones that are pending (from KEI and have not been closed).

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Friday, April 26, 2019 12:00 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: NIH march-ins

A media outlet noticed that the Green Paper says: Although the march-in right has not been used, the National Institutes of Health (NIH) has received 12 requests to initiate march-in proceedings.⁶⁴
Footnote 64: Data provided to NIST by the NIH. Six of the march-in requests and NIH determinations are detailed in: Thomas, John. 2016. March-In Rights under the Bayh-Dole Act. CRS Report No. R44597. Washington, D.C. Congressional Research Service

There are 6 on the OTT website. I don't know where the other 6 came from. Do you?

Mark L. Rohrbaugh, Ph.D., J.D.

REL0000024540

Special Advisor for Technology Transfer
Office of Science Policy
National Institutes of Health

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 3/6/2019 5:46:00 PM
To: Lambertson, David (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3c95b34f709746a8a2553ce54e74ace2-lambertson]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Do you have an example NIH response to KEI on DOJ review?

I have not directly addressed

b5

b5

From: Lambertson, David (NIH/NCI) [E]
Sent: Wednesday, March 06, 2019 12:35
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Subject: RE: Do you have an example NIH response to KEI on DOJ review?

My recollection is that

b5

b5

David A. Lambertson, Ph.D.
Senior Technology Transfer Manager
Technology Transfer Center
National Cancer Institute/NIH
david.lambertson@nih.gov
<http://ttc.nci.nih.gov/>

9609 Medical Center Drive, Rm 1-E530 MSC 9702
Bethesda, MD 20892-9702 (USPS)
Rockville, MD 20850-9702 (Overnight/express mail)
Phone (Main Office): 240-276-5530
Phone (direct): (240) 276-6467
Fax: 240-276-5504

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From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 06, 2019 12:23 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov>
Subject: Do you have an example NIH response to KEI on DOJ review?

REL0000024542

b5

Thx

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Office of Science Policy
National Institutes of Health

From: Joe Allen [jallen@allen-assoc.com]
Sent: 3/20/2018 2:48:46 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Re: Boston Globe: researcher who worked on drug didn't disclose federal funding
Attachments: Boston Globe article KEI Aegerion drug.pdf

The story's attached

On 3/19/2018 6:55 PM, Joe Allen wrote:

Jamie doesn't have any problems getting his articles placed. Since I don't subscribe to The Globe can only pull up the headline and the blurb below that which pretty much tells the tale :
Watchdog group says researcher who worked on Aegerion drug didn't disclose taxpayer funding

The Boston Globe

As a penalty for allegedly failing to disclose the grants, the group asked NIH to take title to the patents, a rarely-used remedy available under the 1980 **Bayh-Dole Act**, which deals with intellectual property arising from federal government-funded research. If NIH took that action, Juxtapid — which was ...

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

REL0000024544



Watchdog group says researcher who worked on Aegerion drug didn't disclose taxpayer funding

By Jonathan Saltzman

GLOBE STAFF MARCH 19, 2018

As if Aegerion Pharmaceuticals didn't have enough problems.

In January, a federal judge penalized the Cambridge biopharmaceutical company for improperly marketing a cholesterol drug, and required some of the \$40.1 million that Aegerion agreed to pay to go to the company's victims.

Now a Washington, D.C.-based watchdog group says an Ivy League professor who helped invent the drug in question, Juxtapid, never disclosed taxpayers' role in his work when he obtained six patents, as required by federal law.

Knowledge Ecology International wrote to the National Institutes of Health that the University of Pennsylvania has received more than \$68 million in grants for research led by Dr. Daniel J. Rader, chairman of the genetics department at the Perelman School of Medicine. At least \$293,000 related to his work on Juxtapid, said the watchdog group.

ADVERTISING

As a penalty for allegedly failing to disclose the grants, the group asked NIH to take title to the patents, a rarely used remedy available under the 1980 Bayh-Dole Act, which deals with intellectual property arising from federal government-funded research.

If NIH took that action, Juxtapid — which was approved in 2012 and costs about \$300,000 a year per patient — would be made available as a generic drug in 2020 instead of 2027, according to James Love, director of Knowledge Ecology International.

“The government is giving people millions of dollars in grants, and they have an obligation to disclose government funding in the invention,” Love said in an interview.

Juxtapid generated more than \$100 million in sales in 2016.

NIH officials said they will review the letter. Neither Rader nor representatives of the University of Pennsylvania responded to requests for comment.

Less than a week ago, the watchdog group wrote a similar letter to federal officials complaining that Gilead Sciences Inc., a California-based biotech, had failed to disclose that one patent on its blockbuster hepatitis C drug, Sovaldi, had been developed with the use of taxpayer funds.

In contrast to Gilead, Aegerion has been a profoundly troubled company.

Federal prosecutors said that after Aegerion received approval from the Food and Drug Administration to market Juxtapid for treating high cholesterol in people with a rare genetic disease, the company promoted the drug for patients who did not have the condition. Many of them suffered side effects including liver toxicity and gastrointestinal distress, prosecutors said.

On Jan. 30, Aegerion pleaded guilty to two misdemeanor counts that it misbranded Juxtapid in violation of the Federal Food, Drug and Cosmetic Act.

Aegerion merged with QLT Inc. in 2016 and became a subsidiary of the newly named Canada-based Novilion.

A spokeswoman for Novilion said company officials weren't familiar with the allegations and had no comment.

Knowledge Ecology International, or KEI, has argued that the high prices of cutting-edge drugs make it even more important for the government to exercise its authority to take title to patents. KEI has also lobbied in favor of requiring drugmakers to publicly disclose how much it costs to develop medicines.

Jonathan Saltzman can be reached at jsaltzman@globe.com

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From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 3/22/2016 6:12:25 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Dft UC Letter
Attachments: UC Request DFT 03222016 ah.docx

Mark: I have attached the draft UC letter. Please let me know if you have any edits, etc. I hope to send this and the draft decision which I will send shortly for your review also, to others this afternoon. Ann

b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 11/20/2018 9:11:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Attachments: NIH to KEI re Ovensa 23NOV2018.docx

See last sentence first paragraph.

beseder?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 16:09
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

b5

b5 Otherwise fine.

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 4:07 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Importance: High

Reviewvez y commentez-vous, s'il vous plait.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 16:03
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

But if it was emailed and not mailed to you, you could respond to the email that they sent you.

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:54 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Importance: High

REL0000024548

That means pdf with our pretty letterhead.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 15:43
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

By the means they were delivered to you.

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Importance: High

Formal letter or email?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 15:39
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

I suggest b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:19 PM
To: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

The Spreader of Love and I have been trading emails about this FR notice for the better part of a week.

b5

Thoughts?

From: James Love <james.love@keionline.org>
Sent: Tuesday, November 20, 2018 15:10
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Brook Baker <b.baker@northeastern.edu>; Alex Lawson <alawson@socialsecurityworks.org>; Allison Love

REL0000024548

<mardiniavon@hotmail.com>; Erin Little <erin.little@sucreblue.org>

Subject: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

Dear Michael Shmilovich

Attached are the joint comments for the notice published in the Federal Register (83 FR 55556), "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)," concerning a prospective exclusive license to Ovensa, a firm located in Canada.

From:

Organizations

HealthGAP

Knowledge Ecology International (KEI)

Social Security Works (SSW)

The Young Professionals Chronic Disease Network (YP-CDN)

Individuals

Allison Love Mardini (type 2 diabetes patient)

Brook K Baker

James Love

--

James Love. Knowledge Ecology International

<http://www.keionline.org>

twitter.com/jamie_love

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 3/19/2018 6:48:16 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Request for NIH to investigate failure to report federal funding in Juxtapid (INN lomitapide)

Thank you Mark. It appears that this involves the University of Pennsylvania and possibly NIH's funding. Assuming you have a copy of the KEI request, I will not send another copy to you.

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, March 19, 2018 2:40 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FW: Request for NIH to investigate failure to report federal funding in Juxtapid (INN lomitapide)

FYI Dale and I both recommended Karen talk/send this to you.

From: Berkley, Dale (NIH/OD) [E]
Sent: Monday, March 19, 2018 12:33 PM
To: Rogers, Karen (NIH/OD) [E] <RogersK@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Roering, Jill (NIH/OD) [E] <roeringj@od.nih.gov>; Goldstein, Bruce (NIH/OD) [E] <goldsteb@mail.nih.gov>
Subject: RE: Request for NIH to investigate failure to report federal funding in Juxtapid (INN lomitapide)

I would think that

b5

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rogers, Karen (NIH/OD) [E]
Sent: Monday, March 19, 2018 10:01 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Roering, Jill (NIH/OD) [E] <roeringj@od.nih.gov>; Goldstein, Bruce (NIH/OD) [E] <goldsteb@mail.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Request for NIH to investigate failure to report federal funding in Juxtapid (INN lomitapide)

Morning Mark – Could you please advise how I should handle this new inquiry from KEI? Funding appears to be related to grants and there is no technology, inventor, CRADA or licensing activity to report from NIH TechTracS. Regards, Karen

Karen L. Rogers
Acting Director
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

REL0000024549

E-Mail: RogersK@nih.gov
Phone: 301-435-4359
Fax: 301-402-8678

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From: Andrew Goldman [<mailto:andrew.goldman@keionline.org>]

Sent: Monday, March 19, 2018 9:49 AM

To: Rogers, Karen (NIH/OD) [E] <rogersk@od.nih.gov>; Roering, Jill (NIH/OD) [E] <roeringj@od.nih.gov>; Goldstein, Bruce (NIH/OD) [E] <goldsteb@mail.nih.gov>

Cc: Jamie Love <james.love@keionline.org>

Subject: Request for NIH to investigate failure to report federal funding in Juxtapid (INN lomitapide)

Dear Ms. Rogers, Ms. Roering, and Mr. Goldstein:

Please see the attached cover letter and memo requesting that NIH investigate and remedy a failure to disclose federal funding in Juxtapid (INN lomitapide).

Please feel free to contact me with any questions.

Sincerely,

Andrew S. Goldman

Counsel, Policy and Legal Affairs

Knowledge Ecology International

andrew.goldman@keionline.org // www.twitter.com/ASG_KEI

tel.: +1.202.332.2670

www.keionline.org

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 9/19/2018 3:18:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: In Re 83 FR 35663; Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors to MTTI
Attachments: NIHtoKEI re MTTI 5Sept2018.pdf

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Wednesday, September 05, 2018 16:00
To: 'James Love' <james.love@keionline.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: In Re 83 FR 35663; Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors to MTTI

Dear Messrs. Love, Abinader and Dr. Ress:

Thank you for your comments to the above referenced FR notice, we have considered them and respectfully enclose our response.

Regards,

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@mail.nih.gov

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"Always be yourself...unless you can be a pirate... then; obviously, be a pirate"

REL0000024552



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
Michael Shmilovich, Esq., CLP
shmilovm@mail.nih.gov

September 5, 2018

James Packard Love
Luis Gil Abinader
Dr. Manon Anne Ress

IN RE: Prospective Grant of Exclusive Patent License: Radiotherapeutics Against
Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (to Molecular Targeting Technologies, Inc.
(MTTI)).

Dear Messrs. Love, Abinader and Dr. Ress:

Thank you for providing us with your comments regarding the aforementioned Federal Register notice. Prior to posting notices of the proposed grant of an exclusive commercial patent licenses, the NIH determines that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) are satisfied and that the company applying for the license is qualified both technically and financially to take on the development of a product in the proposed field based on United States Government owned intellectual property. The notice period provides an opportunity for public comment and possible objection to the proposed license. We consider all comments prior to negotiating the proposed license and have considered your comments.

With regards to this license in particular, after extensive discussions with MTTI and after reviewing their application, which included a comprehensive commercial development plan, we determined that the criteria set forth in 37 CFR 404.7(a)(1)(ii-iii) are satisfied. MTTI demonstrates both the scientific and financial capacity to develop a radiotherapeutic that targets somatostatin-receptor expressing neuroendocrine tumors. In addition, the scope of the license proposed is reasonable and necessary for incentivizing the company to undertake a difficult endeavor such as producing a therapeutic of this kind on balance with the Government's interest in promoting the public health and public access to drugs.

We expect international patent application PCT/US2017/054863, as filed, to be published by the end of April 2019 per the 18-month publication rule (PCT Article 21). International patent application PCT/US2017/031696 having the same inventors and also owned by the United States Government, is related to the instant patent estate in so much as it discloses compounds conjugated to derivatives of Evans Blue but is not specific to the therapeutic MTTI ultimately seeks to produce. The claims filed in both patent applications are broad and may change during prosecution.

Several companies expressed interest in this patent estate and we provided them with copies of the PCT application as filed for evaluation under the provisions of confidentiality nondisclosure agreements that we signed with them. After evaluating the patent applications and corresponding publications (see Appendix A), MTTI was the only company that provided us with an application for a license. To date, there exists an FDA approved radiotherapeutic on the market for the same indication as the intended license.

We have read through and considered the terms and suggestions proffered in your points 1. through 4. If your organization requests more documentation, such requests should be filed under the Freedom of Information Act. The webpage for the NIH FOIA Office provides more information on filing requests <http://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedom-information-act-office/submitting-foia-requests>.

Sincerely,

Michael A. Shmilovich, Esq., CLP

REL0000024552.0001

APPENDIX A – Publication citations

Response to Single Low-dose ^{177}Lu -DOTA-EB-TATE Treatment in Patients with Advanced Neuroendocrine Neoplasm: A Prospective Pilot Study.

Wang H, Cheng Y, Zhang J, Zang J, Li H, Liu Q, Wang J, Jacobson O, Li F, Zhu Z, Chen X.

Theranostics. 2018 May 12;8(12):3308-3316. doi: 10.7150/thno.25919. eCollection 2018.

PMID: 29930731

Safety, Pharmacokinetics and Dosimetry of a Long-Acting Radiolabeled Somatostatin Analogue ^{177}Lu -DOTA-EB-TATE in Patients with Advanced Metastatic Neuroendocrine Tumors.

Zhang J, Wang H, Jacobson Weiss O, Cheng Y, Niu G, Li F, Bai C, Zhu Z, Chen X.

J Nucl Med. 2018 Apr 13. pii: jnumed.118.209841. doi: 10.2967/jnumed.118.209841. [Epub ahead of print]

PMID:29653971

Evans Blue Attachment Enhances Somatostatin Receptor Subtype-2 Imaging and Radiotherapy.

Tian R, Jacobson O, Niu G, Kiesewetter DO, Wang Z, Zhu G, Ma Y, Liu G, Chen X.

Theranostics. 2018 Jan 1;8(3):735-745. doi: 10.7150/thno.23491. eCollection 2018.

PMID: 29344302

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 11/20/2018 9:07:16 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Attachments: NIH to KEI re Ovensa 23NOV2018.docx

Reviewvez y commentez-vous, s'il vous plait.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 16:03
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

But if it was emailed and not mailed to you, you could respond to the email that they sent you.

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:54 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Importance: High

That means pdf with our pretty letterhead.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 15:43
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

By the means they were delivered to you.

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Importance: High

Formal letter or email?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, November 20, 2018 15:39
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>
Subject: RE: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

I suggest:

b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Tuesday, November 20, 2018 3:19 PM
To: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

The Spreader of Love and I have been trading emails about this FR notice for the better part of a week.

Their comments sound like suggestions and not an objection.

I am wondering whether we should feel obliged to respond.

Thoughts?

From: James Love <james.love@keionline.org>
Sent: Tuesday, November 20, 2018 15:10
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Brook Baker <b.baker@northeastern.edu>; Alex Lawson <alawson@socialsecurityworks.org>; Allison Love <mardiniavon@hotmail.com>; Erin Little <erin.little@sucreblue.org>
Subject: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

Dear Michael Shmilovich

Attached are the joint comments for the notice published in the Federal Register (83 FR 55556), "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)," concerning a prospective exclusive license to Ovensa, a firm located in Canada.

From:

Organizations

HealthGAP

Knowledge Ecology International (KEI)

Social Security Works (SSW)

The Young Professionals Chronic Disease Network (YP-CDN)

Individuals

Allison Love Mardini (type 2 diabetes patient)

Brook K Baker

James Love

REL0000024556

--

James Love. Knowledge Ecology International

<http://www.keionline.org>

twitter.com/jamie_love

b5

From: Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DODSONSE]
Sent: 9/24/2015 9:31:48 PM
To: Duberman, Josh (NIH/OD/ORS) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ORS/cn=dubermaj]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]; Reczek, Peter (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Reczekprd1e]; Baden, Elizabeth (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Badenem]
CC: Volkov, Marina (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=nimh/cn=mvolkov]; Rosema, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Rosemals01d]
Subject: RE: Gleevec white paper
Attachments: v1WHITE PAPER Gleevec.v.1_pr MLR_SED.docx

Hi Peter et al,

Thanks for the chance to review. This is really nicely put together. I have added my suggested edits and comments on top of Mark's version.

One logistical thing to consider - since this white paper is so heavily NCI-related, I think we need to recruit an SME from NCI to review and comment.

Cheers,
Sara

From: Duberman, Josh (NIH/OD/ORS) [E]
Sent: Thursday, September 24, 2015 4:27 PM
To: Rohrbaugh, Mark (NIH/OD) [E]; Reczek, Peter (NIH/OD) [E]; Baden, Elizabeth (NIH/OD) [E]
Cc: Volkov, Marina (NIH/OD) [E]; Rosema, Laura (NIH/OD) [E]; Dodson, Sara (NIH/OD) [E]
Subject: RE: Gleevec white paper

Hi – Here are my initial comments on section VIb, below (already sent to Peter) – I will continue checking the rest of the document and get back to you – best - Josh

I checked section VIb as requested,

b5

b5

b5

Josh Duberman, M.L.I.S.
Informationist / Research Librarian
National Institutes of Health Library
Division of Library Services
Office of Research Services
Bldg 10, 1L09K, MSC 1150
Bethesda, MD 20892-1150
T: 301.594.6200 F: 301.402.0254
Cell: [b6] [j.duberman@nih.gov]

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Facebook: <http://www.facebook.com/nihlibrary>
Twitter: <http://www.twitter.com/nihlchem>

Your Partner in Research

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, September 24, 2015 4:22 PM
To: Reczek, Peter (NIH/OD) [E]; Baden, Elizabeth (NIH/OD) [E]; Duberman, Josh (NIH/OD/ORS) [E]
Cc: Volkov, Marina (NIH/OD) [E]; Rosema, Laura (NIH/OD) [E]; Dodson, Sara (NIH/OD) [E]
Subject: RE: Gleevec white paper

I also wanted to add [b5]

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, September 24, 2015 4:11 PM
To: Reczek, Peter (NIH/OD) [E]; Baden, Elizabeth (NIH/OD) [E]; Duberman, Josh (NIH/OD/ORS) [E]
Cc: Volkov, Marina (NIH/OD) [E]; Rosema, Laura (NIH/OD) [E]; Dodson, Sara (NIH/OD) [E]
Subject: RE: Gleevec white paper

See my proposed edits. Overall looks good to me.

From: Reczek, Peter (NIH/OD) [E]
Sent: Friday, September 18, 2015 2:21 PM
To: Rohrbaugh, Mark (NIH/OD) [E]; Baden, Elizabeth (NIH/OD) [E]; Duberman, Josh (NIH/OD/ORS) [E]
Cc: Volkov, Marina (NIH/OD) [E]; Rosema, Laura (NIH/OD) [E]; Dodson, Sara (NIH/OD) [E]
Subject: Gleevec white paper

Hi all...

Attached is the version 1 draft of the Gleevec white paper. Please note that the exec summary and conclusions are not written and the references are incomplete. Have fun editing...hopefully, we'll have a final draft completed by the end of next week (my last day is Sept. 25). In the meantime I'll work on the exec summary and, if anyone would like to take a crack at the "conclusions" please feel free.

Elizabeth....could you provide a fresh copy of Table IV.1 from your files?
?

b5

REL0000024558

Josh...Could you please pay particular attention to section VI.b. We need to be sure of the references.

Thanks,
Peter

Peter R. Reczek, Ph.D.

AAAS Science and Technology Policy Fellow

Office of Science Policy

Office of the Director

National Institutes of Health

6705 Rockledge Drive, Suite 750

Bethesda, MD 20892

Tel: 301.451.4970

Fax: 301.496.9839

email: peter.reczek@nih.gov

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b5

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 9/19/2018 3:02:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Sinotau and MTTI licenses

The licenses or my responses to KEI?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, September 18, 2018 16:35
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Subject: RE: Sinotau and MTTI licenses

Please send me the final when you finish them. Thanks.

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Tuesday, August 28, 2018 9:24 AM
To: Deutch, Alan (NIH/NHLBI) [E] <deutch@nhlbi.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Sinotau and MTTI licenses

Dale, Mark and Alan -- ...same for MTTI... please review.

From: James Love <james.love@keionline.org>
Sent: Monday, August 27, 2018 16:57
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Sinotau and MTTI licenses

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

Dear Michael Shmilovich

Attached are two comments filed jointly by KEI and UACT, regarding licenses noticed in the federal register.

1. Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)
2. Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (<https://www.federalregister.gov/d/2018-16065>)

James Love

REL0000024559

--

James Love. Knowledge Ecology International

<http://www.keionline.org>

twitter.com/jamie_love

From: Hudson, Kathy (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=HUDSONKL]
Sent: 3/22/2016 1:09:03 AM
To: Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]; Hallett, Adrienne (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hallettaa07c]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=jorgensonla]; Baker, Rebecca (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Bakerrg]
Subject: march in letter
Attachments: 1 Letter from 11 NGOs calling for NIH to take action on high drug prices.msg

Fyi attached.

From: Reshma Ramachandran; b6
Sent: 3/21/2016 6:01:55 PM
To: Collins, Francis (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Collinsfr]
CC: Burwell, Sylvia M. (HHS/OS) [/O=NIH/OU=NIH/EXCHANGE/cn=Recipients/cn=Sylvia.Burwell.OS]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Letter from 11 NGOs calling for NIH to take action on high drug prices
Attachments: NGO-xtandi-support-letter-March-21-2016.pdf

Dear Director Collins:

Attached, please find a letter signed by eleven nongovernmental organizations in support of the request by Knowledge Ecology International and the Union for Affordable Cancer Treatment that the NIH use the government's rights in patents on the prostate cancer drug enzalutamide (marketed as Xtandi). We call upon you to hold an open and transparent public hearing to discuss the issues raised by that request and welcome any further discussion.

Sincerely,

Reshma Ramachandran
National Physicians Alliance

—

Reshma Ramachandran, MD MPP

Assistant Scientist (Research Faculty), Environmental Health Sciences
Johns Hopkins Bloomberg School of Public Health
ReAct-Action on Antibiotic Resistance Strategic Policy Program
National Physicians Alliance FDA Task Force Co-Chair

e: **b6**
m:

t: <https://twitter.com/reshmagar>

From: Koniges, Ursula (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D5AE2C3139654BC0B9B95718D516310B-KONIGESUM]
Sent: 3/6/2019 2:11:27 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Ekweani, Elonna (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e57d5fb210184b3c905698fe63ee1f1d-ekweaniej]
Subject: RE: Bloomberg News on new ITIF report

Thanks Mark for sharing this – that’s quite the mis-interpretation by a reporter from a major news organization.

The report author (Stephen Ezell, who gave one of the lectures in the FAES TT course I took during my first PMF year) doesn’t seem to mention the 210 drugs paper. FYI to use Chrome if you’d like to look at the report, as it doesn’t seem to work well with IE.

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, March 05, 2019 1:30 PM
To: Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>; Brandt Hansberger, Patricia (NIH/OD) [E] <brandtp@od.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Koniges, Ursula (NIH/OD) [E] <ursula.koniges@nih.gov>; Ekweani, Elonna (NIH/OD) [E] <elonna.ekweani@nih.gov>; Berger, Adam (NIH/OD) [E] <adam.berger@nih.gov>; Jorgenson, Lyric (NIH/OD) [E] <lyric.jorgenson@nih.gov>
Subject: FW: Bloomberg News on new ITIF report

They got one MAJOR point wrong. The pub showing some NIH funding for the 210 drugs studied by Bentley University primarily is related to basic biological mechanisms that were reported publicly for anyone to advance further. Only if there is a patent on a drug or its use, very few of the 210, funded by NIH, would NIH have authority to use march-in (or the Army in their case).

Federal Drug Patent Grab Means Fewer New Medicines: Think Tank (1)

- Using Bayh-Dole patent law to control drug prices could mean fewer medicines
- Report questioned as drug industry propaganda

By Jeannie Baumann | March 4, 2019 4:13PM ET

(Updated to include comments from PhRMA in the final two paragraphs.)

Fewer new medicines would come onto the market if the NIH exercised its rights to commandeer drug patents as a way of combating high drug prices, according to a think tank.

The report released March 4 from the Information Technology and Innovation Foundation (ITIF) is a win for the drug industry, which continues to face criticism on Capitol Hill for the rising costs of prescription drugs. Lawmakers and the White House are considering a number of policy

options to bring down drug prices, and the use of NIH funds in drug development has come up in recent drug pricing hearings.

Under the Bayh-Dole Act, a federal agency that funded research leading to an invention can “march in” and issue patent licenses on its own—thereby ignoring exclusivity rights—if “reasonable terms are not being met” on drug pricing and if the agency has the intellectual property on the drug’s molecule.

A [study](#) published last year found NIH funding contributed to the development of every new drug approved by the Food and Drug Administration from 2010 to 2016, meaning the NIH could in theory exercise its march-in rights all 210 of those drugs.

Rights Never Used

But the NIH has never exercised its march-in rights. The agency rejected requests for AbbVie’s AIDS drug Norvir and Xtandi, a cancer drug from Astella Pharma and Pfizer Inc.

NIH Director Francis Collins hasn’t ruled out the possibility of using march-in rights for drug pricing but called it an unlikely move for the agency. The NIH is more likely to intervene if a company failed to commercialize a product.

Bayh-Dole is a 1980 patent and trademark law ([Pub. L. 96-517](#)) that aimed to spur innovation by allowing the government to license technologies to the private sector, particularly for university scientists who invented products with federally-funded research grants.

The fact that march-in rights have never been used has contributed to higher drug costs because there’s no pressure on drug companies to lower drug prices when a company has exclusive rights to the drug’s active ingredient, Peter Maybarduk, director of Public Citizen’s Global Access to Medicines Program, told Bloomberg Law.

“If you implement one half of this [Bayh-Dole] regime without the other, of course you’re likely to see extreme price abuse,” Maybarduk said. “There has to be some sort of discipline on price and some sort of disincentive to charging whatever society will pay.”

The ITIF report said using Bayh-Dole for drug pricing would significantly reduce the pace of biopharmaceutical innovation, which could lead to fewer new drugs being developed. The report includes four Bayh-Dole case studies, including Bristol-Myers Squibb’s cancer drug Yervoy, which costs \$30,000 per injection.

Stephen Ezell, lead author of the report and vice president of ITIF, said calls to use march-in rights to control drug prices could allow a government entity to retroactively commandeer

innovations that private-sector enterprises invested hundreds of millions, if not billions, of dollars to create.

“That threat would significantly reduce the pace of biopharmaceutical innovation,” Ezell said in a March 4 statement.

Propaganda Claims

James Love, director of a non-profit that’s petitioned for march-in rights, told Bloomberg Law the report contains “a lot of myth and propaganda.” The threat of march-in rights was used as leverage in 2004 to roll back a 400 percent price increase for Norvir for federal programs, he said.

Love is the director Knowledge Ecology International, which worked with the Union for Affordable Cancer Treatment to ask the NIH and Department of Defense to use its march-in rights for Xtandi. Both agencies ultimately denied the requests. Another march-in rights request for Xtandi is pending at the Army.

“Bayh-Dole did not eliminate march-in rights. March-in rights were included, and extended to any case where a patented invention was not ‘available to the public on reasonable terms,’” Love wrote in a March 4 email.

The drug industry didn’t fund ITIF’s report, a foundation spokesperson told Bloomberg Law. The ITIF released its report in advance of a March 7 briefing on the Bayh-Dole Act’s role in catalyzing life sciences development in the U.S.

It’s unclear whether Congress would use march-in as one of the tools in controlling drug pricing, but several lawmakers have expressed interest in the idea. Rep. Lloyd Doggett (D-Texas) has called for the use of march-in rights for drug pricing in the past.

Reps. Alexandria Ocasio-Cortez (D-N.Y.) and Ro Khanna (D-Calif.) raised concerns at a recent House Oversight Committee hearing about how NIH-funded research contributes to new medicines that the private sector develops. Khanna brought up the 2018 study showing the NIH contributed to all 210 new drugs approved by the FDA. Ocasio-Cortez noted the NIH acts as an “early investor” in the development of new medicines and “then they receive no return on the investment they have made.”

A spokesman for the Pharmaceutical Research and Manufacturers of America, the brand-name drug industry trade group, told Bloomberg Law the march-in authority under Bayh-Dole was never intended to serve as a mechanism for regulating the pricing of any particular product, including prescription medicines.

"Doing so could effectively defeat the purpose of Bayh-Dole," PhRMA spokesman Tom Wilbur said. "As this report shows, circumventing patent rights on medical innovation threatens our country's ability to remain competitive."

To contact the reporter on this story: Jeannie Baumann in Washington
at jbaumann@bloomberglaw.com

To contact the editors responsible for this story: Fawn
Johnson at fjohnson@bloomberglaw.com; Randy Kubetin at rkubetin@bloomberglaw.com

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 12/6/2016 12:23:24 PM
To: Joe Allen [jallen@allen-assoc.com]; Robert Hardy [RHardy@COGR.edu]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Invitation from Jamie Love

I am sure that NIH has a very important meeting/event that day (whatever day it is) and we must attend it. With that said it is an interesting invite and I support the co-opting event.

From: Joe Allen [mailto:jallen@allen-assoc.com]
Sent: Monday, December 05, 2016 3:43 PM
To: Robert Hardy <RHardy@COGR.edu>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: Invitation from Jamie Love

OK, perhaps this Flynn movie will steel your resolve: The Charge of the Light Brigade. The same number of us may return from this adventure (but the odds of getting a memorial poem out of it are not high)...

On 12/5/2016 3:18 PM, Robert Hardy wrote:

Whatever you decide to do I'm sure Mark and I support you 1000% but from a distance. I know I have conflicts that day and I suspect Mark will have some as well.

From: Joe Allen [mailto:jallen@allen-assoc.com]
Sent: Monday, December 05, 2016 3:03 PM
To: Rohrbaugh, Mark (NIH/OD) [E]
Cc: Robert Hardy; Hammersla, Ann (NIH/OD) [E]
Subject: Re: Invitation from Jamie Love

One of my favorite movies when I was a kid was Errol Flynn in They Died With Their Boots On. If I go down shooting, just want to make sure I'm not alone.

Actually I'm going to reply to Jamie that I may have a conflict but to send along more details when he has them worked out. It sounds from his reply that the idea is just being formed, but Jan 13 isn't that far away.

PS: I don't think Jamie will have many fans in the Trump Admn.

On 12/5/2016 1:38 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

What did I ever do to you? ☺

From: Joe Allen [mailto:jallen@allen-assoc.com]
Sent: Monday, December 05, 2016 1:36 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Robert Hardy <RHardy@COGR.edu>; Hammersla, Ann (NIH/OD) [E]

[<hammerslaa@mail.nih.gov>](mailto:hammerslaa@mail.nih.gov)

Subject: Re: Invitation from Jamie Love

Hey, maybe I should suggest to Jamie that he invites you. Sort of like saying that there's more room at the Little Big Horn if you want to ask some friends to ride in with you

Sent from my iPhone

On Dec 5, 2016, at 1:32 PM, Rohrbaugh, Mark (NIH/OD) [E]
[<RohrBauM@OD.NIH.GOV>](mailto:RohrBauM@OD.NIH.GOV) wrote:

Never know. They even continue to use the term "compulsory licensing" incorrectly. The term as used in international trade agreements, where the govt takes action on a privately owned and funded patent, differs from court judgements to remedy a wrong or address antitrust and is quite different from an interest the government has in an invention because it funded it.

From: Robert Hardy [<mailto:RHardy@COGR.edu>]
Sent: Monday, December 05, 2016 12:35 PM
To: Joe Allen [<jallen@allen-assoc.com>](mailto:jallen@allen-assoc.com); Rohrbaugh, Mark (NIH/OD) [E]
[<RohrBauM@OD.NIH.GOV>](mailto:RohrBauM@OD.NIH.GOV); Hammersla, Ann (NIH/OD) [E]
[<hammerslaa@mail.nih.gov>](mailto:hammerslaa@mail.nih.gov)
Subject: RE: Invitation from Jamie Love

You might want to find out who else is on the panel.

It could be a lynching. Or maybe he's trying to co-opt you.

From: Joe Allen [<mailto:jallen@allen-assoc.com>]
Sent: Monday, December 05, 2016 12:32 PM
To: Robert Hardy; Mark Rohrbaugh; Ann Hammersla
Subject: Invitation from Jamie Love

My head is spinning

Sent from my iPhone

Begin forwarded message:

From: Jamie Love [<james.love@keionline.org>](mailto:james.love@keionline.org)
Date: December 5, 2016 at 11:54:09 AM EST
To: jallen@allen-assoc.com
Subject: Jan 13

Dear Joseph Allen,

We are thinking of doing a meeting on compulsory licensing in the United States on Jan 13, and would like to have you on a panel on the Bayh-Dole March-In issues, if you are available and interested in joining.

REL0000024568

Jamie

--

James Love. Knowledge Ecology International
<http://www.keionline.org/donate.html>
KEI DC tel: +1.202.332.2670, US Mobile:
+1.202.361.3040, Geneva Mobile:
+41.76.413.6584, twitter.com/jamie_love

--

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(c) b6
www.allen-assoc.com

From: Joe Allen [jallen@allen-assoc.com]
Sent: 3/5/2019 6:00:02 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: Bloomberg News on new ITIF report

They certainly gave the critics plenty of coverage

Federal Drug Patent Grab Means Fewer New Medicines: Think Tank (1)

- Using Bayh-Dole patent law to control drug prices could mean fewer medicines
- Report questioned as drug industry propaganda

By Jeannie Baumann | March 4, 2019 4:13PM ET

(Updated to include comments from PhRMA in the final two paragraphs.)

Fewer new medicines would come onto the market if the NIH exercised its rights to commandeer drug patents as a way of combating high drug prices, according to a think tank.

The report released March 4 from the Information Technology and Innovation Foundation (ITIF) is a win for the drug industry, which continues to face criticism on Capitol Hill for the rising costs of prescription drugs. Lawmakers and the White House are considering a number of policy options to bring down drug prices, and the use of NIH funds in drug development has come up in recent drug pricing hearings.

Under the Bayh-Dole Act, a federal agency that funded research leading to an invention can “march in” and issue patent licenses on its own—thereby ignoring exclusivity rights—if “reasonable terms are not being met” on drug pricing and if the agency has the intellectual property on the drug’s molecule.

A study published last year found NIH funding contributed to the development of every new drug approved by the Food and Drug Administration from 2010 to 2016, meaning the NIH could in theory exercise its march-in rights all 210 of those drugs.

Rights Never Used

But the NIH has never exercised its march-in rights. The agency rejected requests for AbbVie’s AIDS drug Norvir and Xtandi, a cancer drug from Astella Pharma and Pfizer Inc.

NIH Director Francis Collins hasn't ruled out the possibility of using march-in rights for drug pricing but called it an unlikely move for the agency. The NIH is more likely to intervene if a company failed to commercialize a product.

Bayh-Dole is a 1980 patent and trademark law ([Pub. L. 96-517](#)) that aimed to spur innovation by allowing the government to license technologies to the private sector, particularly for university scientists who invented products with federally-funded research grants.

The fact that march-in rights have never been used has contributed to higher drug costs because there's no pressure on drug companies to lower drug prices when a company has exclusive rights to the drug's active ingredient, Peter Maybarduk, director of Public Citizen's Global Access to Medicines Program, told Bloomberg Law.

"If you implement one half of this [Bayh-Dole] regime without the other, of course you're likely to see extreme price abuse," Maybarduk said. "There has to be some sort of discipline on price and some sort of disincentive to charging whatever society will pay."

The ITIF report said using Bayh-Dole for drug pricing would significantly reduce the pace of biopharmaceutical innovation, which could lead to fewer new drugs being developed. The report includes four Bayh-Dole case studies, including Bristol-Myers Squibb's cancer drug Yervoy, which costs \$30,000 per injection.

Stephen Ezell, lead author of the report and vice president of ITIF, said calls to use march-in rights to control drug prices could allow a government entity to retroactively commandeer innovations that private-sector enterprises invested hundreds of millions, if not billions, of dollars to create.

"That threat would significantly reduce the pace of biopharmaceutical innovation," Ezell said in a March 4 statement.

Propaganda Claims

James Love, director of a non-profit that's petitioned for march-in rights, told Bloomberg Law the report contains "a lot of myth and propaganda." The threat of march-in rights was used as leverage in 2004 to roll back a 400 percent price increase for Norvir for federal programs, he said.

Love is the director Knowledge Ecology International, which worked with the Union for Affordable Cancer Treatment to ask the NIH and Department of Defense to use its march-in rights for Xtandi. Both agencies ultimately denied the requests. Another march-in rights [request](#) for Xtandi is pending at the Army.

"Bayh-Dole did not eliminate march-in rights. March-in rights were included, and extended to any case where a patented invention was not 'available to the public on reasonable terms,'" Love wrote in a March 4 email.

The drug industry didn't fund ITIF's report, a foundation spokesperson told Bloomberg Law. The ITIF released its report in advance of a March 7 [briefing](#) on the Bayh-Dole Act's role in catalyzing life sciences development in the U.S.

It's unclear whether Congress would use march-in as one of the tools in controlling drug pricing, but several lawmakers have expressed interest in the idea. Rep. Lloyd Doggett (D-Texas) has [called for](#) the use of march-in rights for drug pricing in the past.

Reps. Alexandria Ocasio-Cortez (D-N.Y.) and Ro Khanna (D-Calif.) raised concerns at a recent House Oversight Committee [hearing](#) about how NIH-funded research contributes to new medicines that the private sector develops. Khanna brought up the 2018 study showing the NIH contributed to all 210 new drugs approved by the FDA. Ocasio-Cortez noted the NIH acts as an "early investor" in the development of new medicines and "then they receive no return on the investment they have made."

A spokesman for the Pharmaceutical Research and Manufacturers of America, the brand-name drug industry trade group, told Bloomberg Law the march-in authority under Bayh-Dole was never intended to serve as a mechanism for regulating the pricing of any particular product, including prescription medicines.

"Doing so could effectively defeat the purpose of Bayh-Dole," PhRMA spokesman Tom Wilbur said. "As this report shows, circumventing patent rights on medical innovation threatens our country's ability to remain competitive."

To contact the reporter on this story: Jeannie Baumann in Washington at jbaumann@bloomberglaw.com

To contact the editors responsible for this story: Fawn Johnson at fjohnson@bloomberglaw.com; Randy Kubetin at rkubetin@bloomberglaw.com

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From: Frisbie, Suzanne (NIH/NIAID) [E] [/O=NIH/OU=NIHEXCHANGE/CN=NCI/CN=FRISBIES]
Sent: 3/7/2016 6:06:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: response to KEI

That works, Kay Miller will send out an invite with the telecon details.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, March 07, 2016 12:47 PM
To: Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov>
Subject: Re: response to KEI

How about 10 tomorrow?

Sent from my iPhone

On Mar 7, 2016, at 12:35 PM, Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov> wrote:

Great, thank you Mark! The three of us are available except for this afternoon and tomorrow afternoon. Would you be available Tuesday or Wed. morning?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, March 07, 2016 12:33 PM
To: Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov>
Subject: Re: response to KEI

Yes, tomorrow p.m. works

Sent from my iPhone

On Mar 7, 2016, at 12:30 PM, Frisbie, Suzanne (NIH/NIAID) [E] <frisbies@otd.nci.nih.gov> wrote:

Hi Mark,

We were wondering if you might be willing to offer some insight regarding a response to a Federal Register Announcement that NIAID received. The announcement was for the intent to grant an exclusive license. A Mr. Love of KEI (Knowledge Ecology International) posed a number of questions (below), that are not technology transfer related. KEI has posted an interesting blog (<http://keionline.org/node/2421>).

Before drafting a response to KEI, I thought I would check with you to see if there was a standard or template response for such inquiries.

Link to the Federal Register
notice: <https://www.federalregister.gov/articles/2016/02/22/2016-03486/prospective-grant-of-exclusive-license-production-of-attenuated-respiratory-syncytial-virus-vaccines>

Would you be available for a brief chat with Dick Lambert, Rick Williams and myself?

Regards,

Suzanne

Suzanne M. Frisbie, Ph.D.
Deputy Director
Technology Transfer and Intellectual Property Office (TTIPO)
National Institute of Allergy and Infectious Diseases
National Institutes of Health
5601 Fishers Lane
Rockville, MD 20852

Phone: 301-496-2644
Fax: 240-627-3117
www.niaid.nih.gov/ttb/ttb.htm

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Questions being asked by KEI:

1. What provisions exist in the license to protect US residents against excessive or unreasonable pricing?
2. What provisions exist in the license to ensure access in developing countries?
3. What are the royalty arrangements?
4. How much money did the government spend on these inventions? If possible, please provide detailed budgets.
5. How much do you reckon the company receiving the license will have to spend on further development?
6. We request copies of all patent applications related to the specified invention in the notice, including but not limited to the following applications:
 - a. Patent Application Number 61/624,010, filed April 13, 2012,
 - b. Patent Application Number 62/266,199, filed December 11, 2015,
 - c. Patent Application Number 62/105,667, filed January 20, 2015,
 - d. Patent Application Number 62/266,206, filed December 11, 2015.
7. How long has the NIH been developing the technology mentioned in the Notice?
8. Please provide, along with appropriate identifiers and titles, clinical and pre-clinical studies (including any listed on ClinicalTrials.gov or other U.S. government databases), grants, and resulting publications where the NIH participated in developing these technologies.
9. Have there been any phase 1, 2, or 3 clinical trials performed by or in collaboration with the NIH regarding these technologies? In particular, please provide information on any and

all Collaborative Research and Development Agreements (CRADAs) that have been entered into for the development of this technology (including, but not limited to, the CRADAs with Wyeth and Medivance).

From: Deutch, Alan (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=244D755700584812AF36B5E787285647-DEUTCHA]
Sent: 8/30/2018 7:48:57 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Shmilovich, Michael (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7dfe19bfd1d443ceb700b9f22d159a90-shmilovm]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject: RE: Sinotau and MTTI licenses

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, August 30, 2018 3:38 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: RE: Sinotau and MTTI licenses

Ok, b5

b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Thursday, August 30, 2018 3:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: Re: Sinotau and MTTI licenses

Mark— thanks for your comments. I'll modify accordingly. b4,b5

b4,b5

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Thursday, August 30, 2018 at 15:13:37
To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>, "Berkley, Dale (NIH/OD) [E]" <berkleyd@od.nih.gov>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>
Subject: RE: Sinotau and MTTI licenses

Misha:

b5

b5

Thanks
Mark

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Tuesday, August 28, 2018 9:24 AM
To: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Sinotau and MTTI licenses

Dale, Mark and Alan -- ...same for MTTI... please review.

From: James Love <james.love@keionline.org>
Sent: Monday, August 27, 2018 16:57
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Sinotau and MTTI licenses

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

Dear Michael Shmilovich

Attached are two comments filed jointly by KEI and UACT, regarding licenses noticed in the federal register.

1. Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)
2. Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (<https://www.federalregister.gov/d/2018-16065>)

James Love

--

James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love

REL0000024638

From: Reczek, Peter (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=RECZEKPRD1E]
Sent: 9/18/2015 6:20:32 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Baden, Elizabeth (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Badenem]; Duberman, Josh (NIH/OD/ORS) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ORS/cn=dubermaj]
CC: Volkov, Marina (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=nimh/cn=mvolkov]; Rosema, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Rosemals01d]; Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Dodsonse]
Subject: Gleevec white paper
Attachments: v1WHITE PAPER Gleevec.v.1_pr.docx

Hi all...

Attached is the version 1 draft of the Gleevec white paper. Please note that the exec summary and conclusions are not written and the references are incomplete. Have fun editing...hopefully, we'll have a final draft completed by the end of next week (my last day is Sept. 25). In the meantime I'll work on the exec summary and, if anyone would like to take a crack at the "conclusions" please feel free.

Elizabeth....could you provide a fresh copy of Table IV.1 from your files ?

b5

Josh...Could you please pay particular attention to section VI.b. We need to be sure of the references.

Thanks,
Peter

Peter R. Reczek, Ph.D.

AAAS Science and Technology Policy Fellow
Office of Science Policy
Office of the Director
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892
Tel: 301.451.4970
Fax: 301.496.9839
email: peter.reczek@nih.gov

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From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/EXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 4/1/2017 3:11:14 PM
To: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Damianold]; Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=culhane]; Dodson, Sara (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Dodsonse]
Subject: Fwd: Interesting paper on B-D issues
Attachments: PhRMA bayh-dole-act-white-paper-summary.pdf; ATT00001.htm

Sent from my iPhone

Begin forwarded message:

From: "Joe Allen" <jjallen@allen-assoc.com>
To: "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>, "Hammersla, Ann (NIH/OD) [E]" <hammerslaa@mail.nih.gov>
Subject: Interesting paper on B-D issues

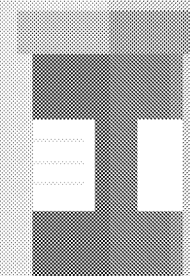
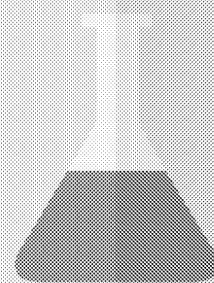
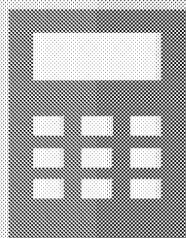
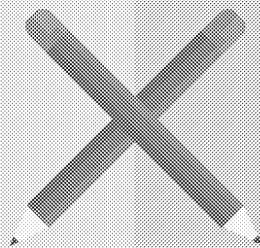
Just came across the attached paper from PhRMA which came out last year. It has some data which I haven't seen before such as documenting the decline in NIH CRADAS when the fair pricing requirement was in force. I did ask them to correct a quote from me describing how a biopharma company lost patent rights to the government before Bayh-Dole, when I described was how inventions were taken from Purdue.

Anyway, you might add this to your stack of information which might come in handy.

--

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HOW THE BAYH-DOLE ACT PROPELLED U.S. GLOBAL LEADERSHIP IN LIFE SCIENCES



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TABLE OF CONTENTS

03	EXECUTIVE SUMMARY
07	INTRODUCTION: ORIGINS OF BAYH-DOLE SPURRED BY CONCERNS ABOUT LOSS OF U.S. GLOBAL COMPETITIVENESS
11	THE BAYH-DOLE ACT: KEY POLICY OBJECTIVES AND PROVISIONS RELATED TO MARCH-IN
16	THE ECONOMIC AND SOCIETAL IMPACT OF BAYH-DOLE: FUELING INNOVATION AND LOCAL ECONOMIES
22	POTENTIAL NEGATIVE IMPACT OF THE USE OF MARCH-IN TO ADDRESS DRUG PRICING
27	CONCLUSION
29	APPENDIX: SUMMARY OF NIH RESPONSES TO MARCH-IN PETITIONS
33	SOURCES

EXECUTIVE SUMMARY

The University and Small Business Patent Procedures Act of 1980 (commonly referred to as “Bayh-Dole”) created the uniform framework that facilitates orderly and efficient technology transfer from universities and other institutions receiving government research funding to the private sector. Bayh-Dole allows universities and other institutions to own title to the patents arising directly from their research activities. With these clear patent rights, universities are then free to license the right to use the most promising technologies to private sector partners in order to commercialize them. As such, Bayh-Dole—which passed with strong bipartisan support—created a viable route by which new insights and valuable research results from universities and other institutions could make their way efficiently to start-up and established firms, who then assume the full risk of development and cost for commercializing the few technologies that eventually prove to be technically and economically viable products.

This paper focuses specifically on the contributions of Bayh-Dole in fostering technology transfer in the life sciences and current threats to this robust framework. Ill-informed proposals to eliminate fundamental aspects of the cooperative academia-industry framework which developed as a result of Bayh-Dole and has been operating successfully for 36 years, or to use this framework to regulate drug prices, reflect a fundamental lack of understanding of the research and development (R&D) process and the benefits that accrue to patients, society, and the economy through the transfer of intellectual property (IP) and the development of innovative treatments.

In the specific case of biopharmaceuticals, together with other factors such as the development of advanced scientific tools and techniques and the emergence of the modern risk-based venture capital market, Bayh-Dole helped lay the foundation for today’s robust biomedical R&D ecosystem and it’s spirit of entrepreneurship which has helped propel U.S. global leadership in the life sciences. The clear and consistent approach to U.S. licensing policy and IP rights established by Bayh-Dole create a predictable mechanism by which early-stage research that is supported in whole or in part by the federal government can attract the

subsequent private sector investment necessary to enable successful commercialization for the benefit of patients, society, and the economy.

Assessments of Bayh-Dole have found it be a vast improvement over the previous state of affairs:

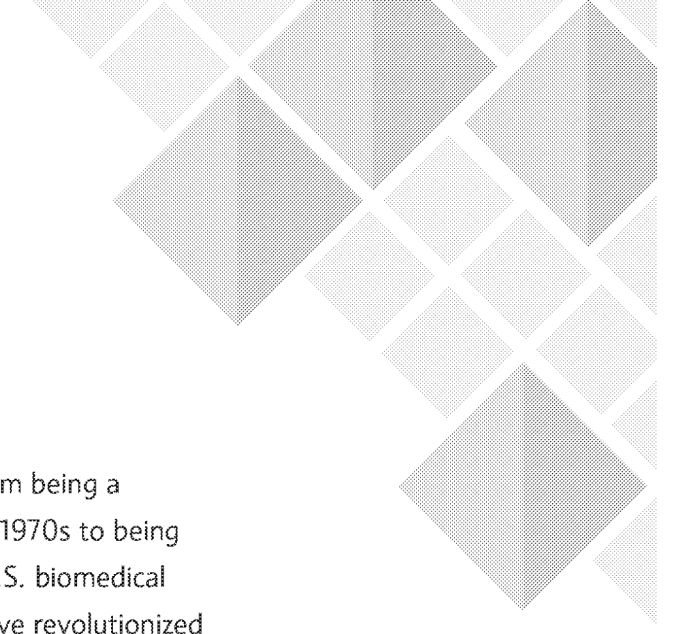
- ▶ Prior to Bayh-Dole, commercialization rates of federally-funded research were estimated to be less than 5%. Since the passage of the law, however, commercialization of federally-funded research has increased dramatically--between 1980 and 2002 alone, U.S. universities generated a tenfold increase in patents.
- ▶ Collaborations between universities and government-funded researchers and the private sector have proven to be a successful model to leverage complementary roles in basic and applied research to support the development of medical innovations and to address unmet patient needs. Without clear patent rights and protections and the economic incentive of exclusive licensing established under Bayh-Dole, private firms would not devote scarce resources to the highly-uncertain development efforts needed to advance research from laboratories receiving public sector funding to the market or the bedside, in the case of medical therapies.
- ▶ Such collaborations and licensing models have been a critical building block of the biomedical R&D ecosystem and the significant contributions it has made to the U.S. economy—and have contributed to the Nation’s competitive advantage in biomedical innovation globally.
- ▶ While collaborations and licensing between academia and the private sector are particularly important to the biomedical R&D ecosystem, they are vital to driving innovation in other industries as well, particularly high-technology industries such as semiconductors. As a result, technology transfer activity has a significant impact on the U.S. economy, with one study finding that between 1996 and 2013, academia-private sector patent licensing across all industries bolstered U.S. GDP by up to \$518 billion and supported up to 3,824,000 U.S. jobs.

- A National Academy of Sciences study found "no reason to believe that either governmental retention of title or routine retention of title by individual inventors would yield more commercial applications or achieve a better balance of the public's stakes" than Bayh-Dole.

To ensure timely and effective commercialization of federally funded research, Congress built in safeguards through a provision of Bayh-Dole that grants the federal agency funding the research a limited right to "march-in" and require the owner of a patent developed through federal funding to grant additional licenses to the technology. This provision is applicable only under certain very limited and specified circumstances, such as if the current licensee fails to make efforts to achieve practical application of the product or fails to reasonably satisfy public health and safety needs (with the latter considered and rejected in the case of manufacturing shortage).

There have been several recent petitions to the National Institutes of Health (NIH) to use march-in rights in an effort to directly reduce the prices of innovative medicines. These misguided efforts threaten to undermine the success achieved under Bayh-Dole over the past 36 years in both fostering early basic research and ensuring the use and translation of those early findings into new medical innovations. The limited march-in right established by the authors of Bayh-Dole reflected an understanding of the inherently costly, risky, and uncertain nature of drug development and the need to provide clear, consistent, and predictable ground rules for government licensing to encourage public and private sector collaborations to harness promising scientific and technological research into advances for patients and consumers. The intent of limited march-in authority was to ensure that grantees were in fact making efforts to commercialize the licensed technology and bring applications to market to the benefit of patients and society.

To date, NIH has considered and denied six march-in petitions. One was the result of a private patent dispute, four claimed that manufacturer pricing was excessive and/or allowed excessive pricing differentials between the U.S. and other countries, and one was intended to address product shortages due to manufacturing difficulties. The NIH has never concluded that licensors had failed to take adequate steps to commercialize the subject inventions. The history and NIH's responses to the six petitions suggest that march-in was never intended to address concerns about drug pricing and could potentially have a chilling



effect on industry willingness to partner with academia and the public sector.

Bayh-Dole is one of the most far-reaching and successful legislative initiatives in contemporary history. Commercial development of federally-supported research has gone from being a major concern in terms of national competitiveness in the 1970s to being a fundamental element of the current, highly successful U.S. biomedical ecosystem. The innovative therapies that have resulted have revolutionized medicine and patients' lives in cancer and many other disease areas, and the economic impacts from technology transfer activities include thousands of new companies founded and millions of jobs supported across the U.S. The threat of march-in as an approach to regulate drug prices would create substantial uncertainty for private sector technology development partners and dramatically alter the framework that has contributed to the growth and sustainability of the robust U.S. R&D ecosystem. At a time when the science has never been more challenging or the potential for fundamentally altering disease processes more promising, public policies should support critically needed public-private collaborations, rather than undermine the future of technology transfer and the U.S. biomedical R&D enterprise that is the envy of the world.

INTRODUCTION: ORIGINS OF BAYH-DOLE SPURRED BY CONCERNS ABOUT LOSS OF U.S. GLOBAL COMPETITIVENESS

“Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole Act of 1980. Together with amendments in 1984 and augmentation in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers’ money. More than anything, this single policy measure helped to reverse America’s precipitous slide into industrial irrelevance.”

—*The Economist*, December 2002

Before the passage of the University and Small Business Patent Procedures Act (commonly referred to as “Bayh-Dole”) in 1980, there was no clear and coordinated patent ownership or exclusive licensing policy across federal agencies. In order to obtain title rights to an invention resulting from federally funded research and development (R&D), grantees such as universities, could request a waiver either in advance during contract negotiations, or on a case-by-case basis after disclosure of the invention to the federal agency sponsoring the research, but the process was inconsistent and unpredictable.

As later Government Accountability Office (GAO) reports summarized, “Those seeking to use government-owned technology found a maze of rules and regulations set out by the agencies in question because there was no uniform federal policy on patents for government-sponsored inventions or on the transfer of technology from the government to the private sector,”¹ and “at the time the bill was considered, 26 different federal agency policies existed regarding the use of results from federally funded research.”²

Not only did federal agency policies vary in whether they permitted university ownership, but the licenses granted were non-exclusive licenses. As a result, there were disincentives for researchers, particularly in the life sciences, to participate in federally-sponsored research. Recalls Joseph Allen (then a staffer to Sen. Birch Bayh, one of the two primary sponsors of Bayh-Dole), a biopharmaceutical company "had several promising government-funded inventions taken away under existing federal patent policies. They explained that taking early stage inventions from their creators, making them widely available through non-exclusive licenses doomed the technology's development."³ Indeed, as co-sponsor of the bill, Senator Robert Dole stated in July 2005, the Government's "track record of promoting the adoption of new university-born technologies by industry during the 1960's and 1970's was dismal. The failure to capitalize on the knowledge that resulted from Federal funding of basic research delayed innovations and denied the benefits of further development, disclosure, exploitation, and commercialization to the American people."⁴

Bayh-Dole was conceived as an effort to ensure that promising technologies funded by the federal government would not sit on the shelf, but could be developed into useful, sometimes life-saving, products for Americans.

Moreover, federal agencies had limited incentives and expertise with which to pursue commercialization on their own. A National Research Council report identified the gap: "In the pre-1980 system of government ownership of inventions arising from federally-funded research—whether in government laboratories, universities, or companies—the incentives to pursue further development and commercialization were severely attenuated and the capacity to do so severely limited. Government agencies, in particular, had no incentive and negligible capacity."⁵

This created, in turn, a lack of incentives for university grantees to invest in commercialization infrastructure: "Where research performers had the possibility of persuading federal agencies to transfer rights to them, the uncertainty of success and


THE PROCESS OF TECHNOLOGY TRANSFER UNDER BAYH-DOLE



the complexities of obtaining waivers of government ownership under different agency rules were often high. Most institutions had no reason to hire specialized personnel and create administrative units to handle these matters.”⁶

As a result of the lack of title to inventions for federal grantees (and the associated patent protection critical to commercial value), companies had little incentive to invest the significant time and money required to translate the basic research into a successful marketable product.⁷ As one government report noted, “at the present time, the Government frequently takes title to inventions produced from research supported by Federal funds...the Federal Government currently has title to some 28,000 patents. Many of these patents are on inventions of great potential economic impact. However, only about five percent of federally owned patents are utilized in the private sector.”^{8,9}

Bayh-Dole was conceived as an effort to ensure that promising technologies funded by the federal government would not sit on the shelf, but could be developed into useful, sometimes life-saving, products for Americans. In 2004, Senator Birch Bayh recalled the intent of Congress in enacting the Bayh-Dole Act, highlighting a perceived loss of national competitiveness, a need



to provide additional incentives for investments in innovation, and a means by which to reap the benefits of federal investments in R&D already made. As he noted, "by the late 70s, America had lost its technological advantage... Since the government refused to permit ownership of the patents, private industry and business refused to invest the resources necessary to bring the products to consumers. As Thomas Edison said: 'Invention is 1% inspiration and 99% perspiration.' With regard to publicly funded research, government typically funds the inspiration and industry the perspiration."

THE BAYH-DOLE ACT: KEY POLICY OBJECTIVES AND PROVISIONS RELATED TO MARCH-IN

The Bayh-Dole Act provided the first-ever comprehensive framework regarding technology transfer from government-funded research at universities and other institutions to the private sector in an effort to encourage the development of promising inventions. The House Committee on the Judiciary described the intent of the proposed legislation as creating a "single, uniform national policy designed to cut down on bureaucracy and encourage private industry to utilize government financed inventions through the commitment of the risk capital necessary to develop such inventions to the point of commercial application."¹⁰ The stated policy objectives in the Bayh-Dole Act are to:

- (U)se the patent system to promote the utilization of inventions arising from federally supported research or development;
- to encourage maximum participation of small business firms in federally supported research and development efforts;
- to promote collaboration between commercial concerns and nonprofit organizations, including universities;
- to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery;
- to promote the commercialization and public availability of inventions made in the United States by United States industry and labor;
- to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.¹¹

11 THE BAYH-DOLE ACT: KEY POLICY OBJECTIVES AND PROVISIONS RELATED TO MARCH-IN

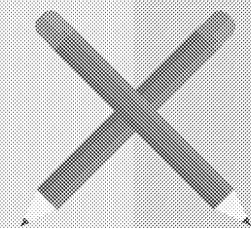
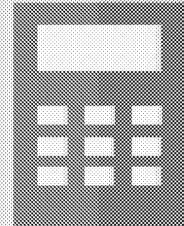
Bayh-Dole does not automatically grant universities and other recipients of federal research funding title to the inventions they discover. They may assert as a matter of right (except in "exceptional circumstances") title to patents on inventions they create using that funding, but they also must meet certain obligations, including filing for patent protection (for patentable inventions), sharing a portion of license revenue with the inventor(s), and meeting certain reporting and disclosure requirements. As a result, universities and other

In fact, as a 2012 Congressional Research Service report notes, "one of the major factors in the reported success of the Bayh-Dole Act is the certainty it conveys concerning ownership of intellectual property."

institutions often invest a significant amount of staff time and other resources to pursue patenting and later, technology transfer, of federally funded inventions. Universities and others are incentivized to make these investments on the basis that they will be able retain full title to those patents (aside from certain narrow reserved rights by the government) and can seek licensing opportunities with industry, to help recoup those costs, fund research and education needs, and support universities' missions of advancing discovery and the social benefits of new knowledge. In fact, as a 2012 Congressional Research Service report notes, "one of the major factors in the reported success of the Bayh-Dole Act is the certainty it conveys concerning ownership of intellectual property."¹²

BENEFITS OF TECHNOLOGY TRANSFER TO UNIVERSITIES:

- ▶ Supports local economic development through the formation of new start-ups and jobs.
- ▶ Helps universities fulfill their broader missions to address societal problems.
- ▶ Increases potential for funding new research through the generation of licensing income and increased opportunities to receive interdisciplinary grants, funding from sources requiring a commercial partner (i.e. through the Small Business Innovation Research program), and by facilitating international research relationships.
- ▶ Promotes a culture of innovation and entrepreneurship among faculty and students.
- ▶ Provides students with valuable opportunities to participate in research with potentially profound real-world applications.



The government does, however, retain certain limited rights. Under Section 203 of the Act, the government has a limited right to “march in” and “require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself.”¹³

The objective of march-in authority was to ensure that the federal investments in innovation in fact made their way into commercialization activities.

Consequently, to exercise “march-in” authority, the relevant federal agency must determine that:

- ▶ The contractor has not made, and is not expected to make, efforts to commercialize the invention within an agreed upon time frame;
- ▶ Public health or safety needs are not reasonably satisfied by the contractor or licensee;
- ▶ The use of the invention is required by the federal government and the contractor or licensee cannot meet the government’s requirements; or
- ▶ The owner of an exclusive license has not obtained certain necessary waivers, or met related requirements.

Since the passage of Bayh-Dole, there have been six instances of petitions requesting the exercise of march-in rights in connection with NIH-funded research relating to a biopharmaceutical product. These petitions have claimed that either licensing activity did not address public health or safety needs or that manufacturer pricing was excessive, for various reasons:

- ▶ One claimed, as a result of a private patent dispute, that the licensor had failed to take steps to achieve practical application (CellPro, 1997);
- ▶ Four claimed that manufacturer pricing was excessive and/or allowed excessive pricing differentials between the U.S. and other countries (Norvir®, 2004; Norvir® 2012; Xalatan®, 2004; Xtandi®, 2016); and
- ▶ One was intended to address product shortages due to manufacturing difficulties (Fabrazyme®, 2010).

All of these march-in petitions have been denied, with the NIH consistently concluding that the products had reached practical application and met health or safety needs and/or “that the extraordinary remedy of march-in is not an appropriate means of controlling prices.”¹⁴ In denying the 1997 CellPro petition, NIH noted that to approve it would “have far-reaching repercussions on many companies’ and investors’ future willingness to invest in federally

“NIH continues to agree with the public testimony in 2004 that the extraordinary remedy of march-in is not an appropriate means of controlling prices of drugs broadly available to physicians and patients.”
—National Institutes of Health, 2013

funded medical technologies.”¹⁵ In denying the 2012 petition, NIH found that, “We do not think that the AbbVie pricing policies and pricing disparities between the United States and other countries trigger any of the four Bayh-Dole march-in criteria,” and more generally, “NIH continues to agree with the public testimony in 2004 that the extraordinary remedy of march-in is not an appropriate means of controlling prices of drugs broadly available to physicians and patients.”¹⁶ In denying the 2016 Xtandi® march-in petition, NIH noted that the medicine had reached “practical application” in that it was “broadly available as a prescription drug.”¹⁷

A summary of NIH responses to march-in petitions is available in the Appendix.



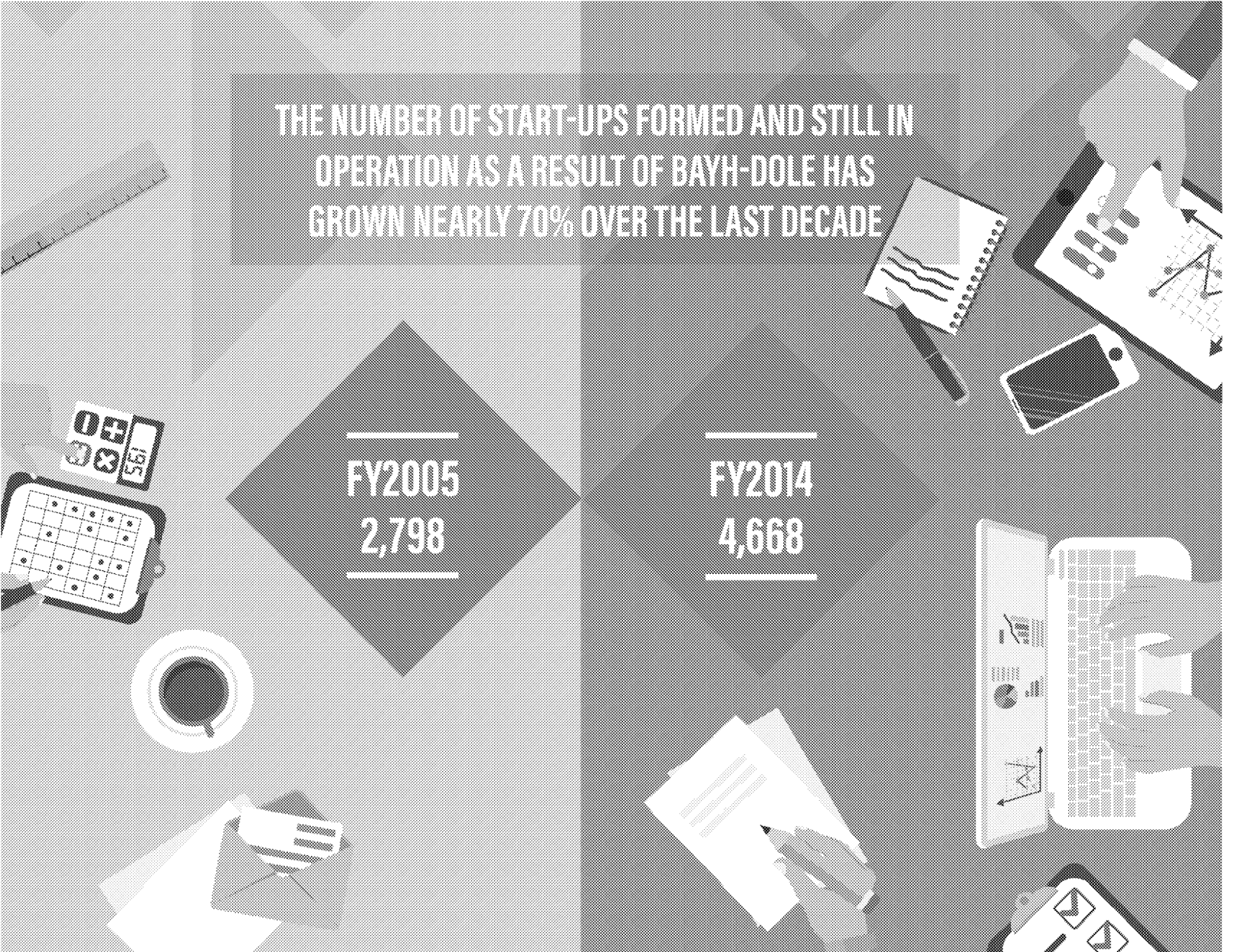
THE ECONOMIC AND SOCIETAL IMPACT OF BAYH-DOLE: FUELING INNOVATION AND LOCAL ECONOMIES

By any measure, the Bayh-Dole Act has had a tremendous impact on the national economy over the nearly four decades since its passage. Its economic contributions can be measured by an increase in the rate of commercialization of university-based technologies through patenting, licensing, research joint ventures, and the creation of startups in all industries. According to one study, university patenting across all technology areas has increased ten-fold since the passage of Bayh-Dole—in 1980, universities were awarded 390 patents; in 2009, the corresponding figure was 3,088.¹⁸ The Association of University Technology Managers (AUTM) undertakes an annual survey of licensing professionals and reports several measures of technology transfer. According to the AUTM data, between 2005 and 2014, all measures of technology transfer activity had increased significantly and hundreds of new start-up companies had been formed as a direct result of Bayh-Dole.¹⁹

BAYH-DOLE TECHNOLOGY TRANSFER ACTIVITY AMONG UNIVERSITIES AND INSTITUTIONS ACROSS ALL TECHNOLOGY AREAS

SELECTED TECHNOLOGY TRANSFER METRICS	FY2005	FY2014
U.S. PATENTS ISSUED	3,278	6,363
LICENSES EXECUTED	4,178	5,435
TOTAL LICENSE INCOME TO UNIVERSITIES FROM TECH TRANSFER	\$2.1 BILLION	\$2.7 BILLION
START-UP COMPANIES FORMED	451	909

Source: Statistics Access for Tech Transfer Database, Association of University Technology Managers, 2016.



THE NUMBER OF START-UPS FORMED AND STILL IN
OPERATION AS A RESULT OF BAYH-DOLE HAS
GROWN NEARLY 70% OVER THE LAST DECADE

FY2005
2,798

FY2014
4,668

Source: Statistics Access for Tech Transfer Database, Association of University Technology Managers, 2016.

University research and start-up companies, which rely on Bayh-Dole's incentives and a partnership model between academia and the private sector, have become an engine for regional economic performance and growth. The importance of start-up firms to regional and national job creation is substantial—it has been estimated elsewhere that start-up businesses are a key driver of job growth, accounting for 70% of gross job creation.²⁰ As AUTM's President, David Winwood has noted, "when academic research yields a new idea, that idea often leads to a new startup company and then to new products in the marketplace. These ideas have the capacity to save lives, improve the way we work and play, and boost local economies—from seed varietals for our farmers to improved treatments for obesity and

diabetes. Time and again these companies blossom, grow and stay in our local communities enhancing economic development.”²¹

Bayh-Dole’s impact on start-up activity across all industries is substantial:

- ▶ In 2014, 909 startup companies were formed as a result of Bayh-Dole and technology transfer activities, 702 of them having their primary place of business in the licensing institution’s home state.²²
- ▶ 11,210 startup companies were reported as having been formed between 1980 and 2014 as a result of technology transfer activities--in 2014 alone, these firms along with other Bayh-Dole licensees introduced over 960 products across a range of technologies.²³
- ▶ Universities create an average of more than two start-up companies each day, and these university-based start-ups have longer life spans and raise more capital than non-university-affiliated start-ups, meaning they support job creation and sustained economic benefits to local economies.²⁴

More specific to the life sciences industry, Bayh-Dole has become a critical element in the rise of “biotech clusters” (i.e. geographic concentrations of biotech firms actively exchanging expertise, human capital and infrastructure, often located near or including universities) and other mechanisms that help pave the way for technology transfer from academia to industry. As summarized by one researcher, “In recent years, there has been a substantial rise in the rate of commercialization of university-based technologies—through patenting, licensing, research joint ventures, and the formation of startup companies. We have also witnessed an increase in investment in science parks and other property-based institutions that facilitate the transfer of technology from universities to firms...most commentators attribute a substantial portion of this activity to the Bayh-Dole Act of 1980, which dramatically changed the incentives of U.S. universities to commercialize their intellectual property. Bayh-Dole instituted a uniform patent policy across federal agencies, removed many restrictions on licensing, and most importantly, allowed universities, rather than the federal government, to own patents arising from federal research grants.”²⁵

While collaborations and licensing between academia and the private sector are particularly important to the biomedical R&D ecosystem, they are vital to driving innovation in other

industries as well, particularly high-technology industries such as semiconductors.²⁶ Overall, the licensing activity spurred by Bayh-Dole has been estimated to have contributed up to \$518 billion to GDP and supported up to 3.8 million jobs in the U.S. between 1996 and 2013 across all industries.²⁷

The enormous economic impact of Bayh-Dole rests on its contributions to society through the commercialization of technologies. By allowing for patent assignment and exclusive licensing, Bayh-Dole enables the private sector to effectively apply early insights from universities and other research institutions to develop the next generation of treatments and cures for patients. Indeed, studies have characterized the roles of industry and academia in the innovation process as complementary. University research, supported by grants and contracts from the public, non-profit, and private sectors is typically focused on the basic research stage (e.g., identification of biochemical mechanism(s) in disease etiology, potential targets). Private sector investment is more heavily concentrated in subsequent stages of pre-clinical development and clinical testing to obtain FDA approval (e.g., medicinal chemistry, process and formulation science, pharmacokinetics and metabolism modeling, and clinical trials to demonstrate safety and efficacy).

Overall, the licensing activity spurred by Bayh-Dole has been estimated to have contributed up to \$518 billion to GDP and supported up to 3.8 million jobs in the U.S. between 1996 and 2013 across all industries.

Researchers have estimated that as a result, 67% to 97% of drug development research is conducted by the private sector.²⁸ Basic research represents only a small portion of the total investment required to bring an idea from “the bench to the bedside”; without clear rules and incentives for industry to partner in undertaking risky drug development, many promising insights would be left “stranded in the lab.” According to the Congressional Research Service, “While basic research is often important to innovation, studies have shown that, on average, it constitutes only 25% of the cost of commercializing a new

technology or technique, thus requiring the expenditure of a substantial amount of additional resources to bring most products or processes to the marketplace.”²⁹

But without the potential for patent assignment and exclusive licensing, private firms would be unlikely to make substantial investments in uncertain and lengthy drug development programs. Thus, Bayh-Dole provided the incentives and framework needed to facilitate academia-industry partnerships to drive initial insights from university labs, to clinical development by industry, and ultimately into FDA-approved medicines that can help patients live longer, healthier lives. In fact, by the mid to late 1990s, over 90% of life science companies in the U.S. had a cooperative relationship with universities.³⁰ Together with other mechanisms, university patenting and licensing is needed for effective knowledge transfers between academia and the private sector.

Concrete examples of the societal benefits from Bayh-Dole licensing of university-based research, when combined with further development by the private sector, include a number of important biopharmaceutical therapies including new vaccines, treatments for costly and burdensome chronic diseases, and innovative new approaches to treating complex diseases such as cancers and HIV.³¹ While the basic underpinnings of these therapies were discovered in universities, biopharmaceutical companies could not have invested the significant resources needed to further develop them into actual FDA-approved medicines without Bayh-Dole. A review of the development histories and relative R&D contributions by the public and private sector for 35 important drugs found that the scientific contributions of the private sector were crucial to all of them. The central scientific contribution by the private sector was evident in all categories of development (basic science, applied science, and clinical, delivery and manufacturing improvements), being most significant in applied science, followed by contributions to enhancing clinical performance and improving commercial production.³² These findings were confirmed by a subsequent analysis by some of the same researchers of 26 individual drugs, drug classes and a combination therapy identified by a previous analysis as “most transformative drugs of the past 25 years.”³³

As several independent government assessments of Bayh-Dole have found, the legislation has achieved its core objective of increasing technology transfer from academia to the private sector:

- ▶ National Academy of Science (NAS): "The Bayh-Dole Act is a sound and flexible framework for promoting the commercialization of university-developed inventions resulting from federally sponsored research...The committee has no reason to believe that either governmental retention of title or routine retention of title by individual inventors would yield more commercial applications or achieve a better balance of the public's stakes."³⁴
- ▶ Congressional Research Service (CRS): "Observers generally agree that the Bayh-Dole Act has successfully met its objectives... The government receives a significant payback through taxes on profits and society benefits from new jobs created and expanded productivity."³⁵
- ▶ Government Accountability Office (GAO): "University administrators and small business representatives whom we interviewed stated that federal patent policy changes since 1980 have had a significant positive impact on their research and innovation efforts... Officials within the agencies and universities we visited said the act was having a positive impact and was working as the Congress intended. They believed that the universities and researchers were receiving greater benefits from their inventions and were transferring technology better than the government did when it retained title to inventions."³⁶

“Observers generally agree that the Bayh-Dole Act has successfully met its objectives... The government receives a significant payback through taxes on profits and society benefits from new jobs created and expanded productivity.”
—Congressional Research Service (CRS)

POTENTIAL NEGATIVE IMPACT OF THE USE OF MARCH-IN TO ADDRESS DRUG PRICING

Expanding the use of march-in rights for purposes other than those intended by the legislation would reverse current exclusive licensing models, and in essence constitute government price controls in certain circumstances, ultimately undermining the careful balance and successful synergy between early public-funded basic research by universities and other institutions and the subsequent substantial and long-term risk-based R&D investments by the private sector. This synergistic relationship relies on clear, consistent and predictable "ground rules" for licensing of government-funded technologies.

These recent proposals harken back to objections to the Bayh-Dole framework at the time of passage. Senator Bayh summarized the arguments of "well-intentioned voices," who argued, "If the taxpayer funds the research, the taxpayer should own the ideas produced" and his response --"However, the result of this policy was billions of taxpayer dollars spent on thousands of ideas and patents which were collecting dust at the PTO. The taxpayers were getting no benefit whatsoever."

The intent of march-in authority was to ensure that grantees were in fact making efforts to commercialize the licensed technology and bring inventions to market to the benefit of patients and society. All five "march-in" petitions decided by NIH to date have been denied, with findings that licensors in fact have taken steps to commercialize the technologies, that "any licensing plan that might result from such a proceeding would not, in our judgment, address the problem" (i.e., product shortage relating to manufacturing technology challenges), or that "because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by the NIH, the NIH believes that the extraordinary remedy of march-in is not an appropriate means of controlling prices."³⁷

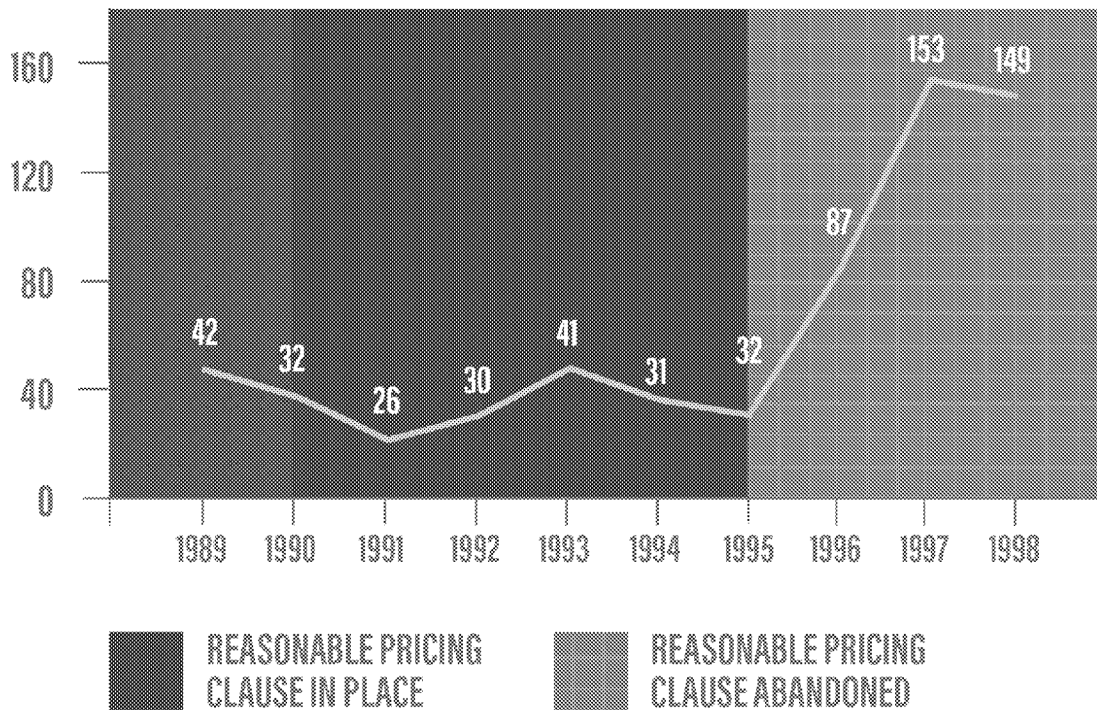
In addition to practical considerations of whether march-in authority would prove to be effective in the case of a public health emergency, based on interviews with agency personnel and other expert stakeholders, the GAO previously identified a fundamental concern relating to the potential impact of march-in authority exercise: "the potential 'chilling effect' that such an action might have could deter investors from investing in the commercialization of the research results and some researchers from participating in federal research efforts."³⁸

Indeed, experience with the NIH's previous failed effort to influence drug pricing by placing conditions on patent licensing agreements suggests that expanding the use of march-in to address drug pricing could chill academia-industry collaboration and the innovation generated from those interactions. In 1989, the NIH adopted a policy of requiring a "reasonable pricing" clause in its Cooperative Research and Development Agreements (CRADAs) between NIH intramural laboratories and private sector partners involving exclusive licenses. Under the policy, exclusive licenses to the private sector for discoveries funded in part by the NIH required that there be "a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public."³⁹ While well-intentioned, the policy resulted in unintended negative consequences harmful to scientific collaboration and the public: "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public."⁴⁰ Given NIH's mission to provide scientific leadership to the nation by "seek(ing) fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability,"⁴¹ diversion of its scarce resources into setting, monitoring, and evaluating the effects of what were in effect price controls in a complex biopharmaceutical discovery and development ecosystem was counterproductive.

Creating unsustainable uncertainty for the private sector, the process involved NIH making a "fair" pricing determination for a medicine only after a company had spent years of effort and millions in financial investment to complete development and begin commercializing the medicine. As a result, CRADAs flat-lined between 1990 and 1994 at approximately 30 per year, as industry was deterred from collaborating with NIH.⁴² Following public hearings with various stakeholders from both the public and private sectors, the NIH removed the reasonable pricing requirement for CRADAs in 1995, and "(t)he effect of abandoning the

clause was immediate. Subsequent to rescission of the clause in April 1995, the number of CRADAs executed by NIH increased substantially”, reaching five times the 1990-94 level, or over 150 in 1997.⁴³ Given the chilling effect on public-private collaborations as a result of NIH’s failed attempt to influence pricing of biopharmaceutical products under the Act through constraining licensing agreements, NIH has not pursued similar approaches since. There is no reason to believe that expanding the use of march-in rights under Bayh-Dole to control drug prices would have any different effect.

REMOVAL OF NIH “REASONABLE PRICING” POLICY LEADS TO RISE IN PUBLIC-PRIVATE COLLABORATIONS



The GAO also identified another potential concern with the exercise of march-in authority: “commercial products or processes based on federal inventions sometimes employ multiple patents, some of which are not federally funded. Such circumstances often pose difficult, if not intractable, issues that could make marching in unattractive for federal officials seeking to commercialize an invention...federal agencies may only have the authority to

march in on one aspect of a product or process, yet marching in may negatively affect the value of all the other patented inventions associated with the product or process."⁴⁴ This is particularly true in the case of biopharmaceutical products, where there may be multiple patents on various aspects of a medicine, including the composition of the active ingredient, the method of use of the medicine, the technology or methods used to produce it, and its dosage form. In cases where a government-funded patent is only one of a set of patents related to a product, the use of march-in may not result in any more timely access to the medicine, yet the use of march-in would nevertheless create significant uncertainty for licensors who, having spent the time and resources needed to develop the government-funded patented technology into FDA-approved medicines, may likely be unwilling to do so again.

In cases where a government-funded patent is only one of a set of patents related to a product, the use of march-in may not result in any more timely access to the medicine...

The uncertainty created by expanding the use of march-in to address pricing concerns undermines the fundamental intent of Bayh-Dole. When universities make investments to secure patent protection for their government-funded inventions and license them to industry, it is with the assumption they will be able to recoup these costs and fund future technology transfer, research, and educational activities that result in new innovations, new companies, and new jobs. When the private sector agrees to license promising, yet early, technologies from academia or other entities that have received federal funding and invest significant financial and other resources into developing and testing those technologies, it is under the assumption that it will have the opportunity to recoup these investments without the added risk of arbitrary and unanticipated government action. Indeed, as a 2012

Congressional Research Service report found, "one of the major factors in the reported success of the Bayh-Dole Act is the certainty it conveys concerning ownership of intellectual property."⁴⁵ Undermining this certainty by marching into a company's exclusive license to a federally-funded patent after it has made significant investments to develop and commercialize the product would drive the private sector away from technology transfer agreements under Bayh-Dole, to the detriment of patients, consumers and the economy.

CONCLUSION

Reviewing others' assessments of the far-ranging impact of the law, Senator Bayh noted in his remarks to NIH opposing march-in, "Changes to Bayh-Dole should be made only after giving careful consideration to what has been accomplished by those who have utilized the provisions of the law. In calling the Bayh-Dole Act "possibly the most inspired piece of legislation to be enacted in America over the past half century," The Economist estimated that the law "created 2,000 new companies, 260,000 new jobs, and now contributes \$40 billion annually to the U.S. economy [across all industries]. This assessment was made almost six years ago and more progress has been made since then."⁴⁶

Senator Bayh's perspective is no less true today – Bayh-Dole is one of the most far-reaching and successful legislative initiatives in contemporary history. Commercial development of federally-supported R&D investments has gone from being a major concern about U.S. national competitiveness in the 1970s to being a fundamental element of the growth and sustainability of the nation's biopharmaceutical research ecosystem—which leads the world today. The innovations that have resulted have furthered medicine and extended patients' lives in cancer and many other costly and challenging disease areas.

Bayh-Dole has been so effective that in 2006, the U.S. House of Representatives unanimously passed a resolution (H. Con. Res. 319) extolling the contributions of the Act to the U.S. economy:

"Resolved by the House of Representatives (the Senate concurring), That it is the sense of the Congress that—

(1) the Bayh-Dole Act (Public Law 96–517) has made substantial contributions to the advancement of scientific and technological knowledge, fostered dramatic improvements in public health and safety, strengthened the higher education system in the United States, served as a catalyst for the development of new domestic industries that have created tens of thousands of new jobs for American citizens, strengthened States and local communities across the

country, and benefitted the economic and trade policies of the United States; and

(2) it is appropriate that the Congress reaffirm its commitment to the policies and objectives of the Bayh-Dole Act by acknowledging its contributions and commemorating the silver anniversary of its enactment."⁴⁷

Without the Bayh-Dole Act's clear, consistent, and predictable framework for patent assignment and the right to enforce and exclusively license these patent rights, private companies likely would not invest in the extensive, risky process of commercializing government-funded technologies into medicines and other therapies for use by patients. The federal government's "march-in" rights under Bayh-Dole were intended to ensure that private firms made adequate efforts to in fact develop the technologies they licensed. March-in was never intended to address concerns about drug pricing, which are more appropriately addressed by other initiatives and approaches (for instance, that eliminate barriers to opportunities for payers and innovators

to jointly develop approaches that reward and incent therapy value). Expanding the use of march-in to address drug pricing would have a chilling effect on essential public-private sector collaborations, to the detriment of the U.S. economy and national competitiveness, and most importantly, to the detriment of patients who are counting on the collective efforts of the public and private sector to make progress against our most costly and challenging diseases.

109TH CONGRESS
1ST SESSION

H.R. 319

Resolved by the House of Representatives (the Senate concurring),
That it is the sense of the Congress that—

IN THE HOUSE OF REPRESENTATIVES
DECEMBER 16, 2005

A BILL

(1) the Bayh-Dole Act (Public Law 96-517) has made substantial contributions to the advancement of scientific and technological knowledge, fostered dramatic improvements in public health and safety, strengthened the higher education system in the United States, served as a catalyst for the development of new domestic industries that have created tens of thousands of new jobs for American citizens, strengthened States and local communities across the country, and benefitted the economic and trade policies of the United States; and (2) it is appropriate that the Congress reaffirm its commitment to the policies and objectives of the Bayh-Dole Act by acknowledging its contributions and commemorating the silver anniversary of its enactment.

APPENDIX: SUMMARY OF NIH RESPONSES TO MARCH-IN PETITIONS

- **Petition by CellPro calling for march-in, asserting that Baxter Healthcare Corporation failed to commercialize certain stem cell patents (filed March 3, 1997; denied August 1, 1997).**

In a patent dispute with The Johns Hopkins University and Baxter Healthcare Corporation, CellPro, Inc. petitioned NIH to exercise its march-in rights in connection with certain patents relating to stem cell separation methods owned by The Johns Hopkins University and licensed first to Becton-Dickinson and then to Baxter Healthcare Corporation. CellPro claimed Baxter had failed to take effective steps to achieve practical application of the subject inventions: "Baxter has threatened to require CellPro to remove the Ceprate products from the market on the basis of patents issued to Johns Hopkins that are governed by the Bayh-Dole Act."⁴⁸

NIH denied the petition, determining that Baxter "met the statutory and regulatory standard for practical application" as evidenced by its "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public", further finding that "Hopkins and Baxter have taken, or are expected to take within a reasonable time, effective steps to achieve practical application of the applicable patents ...and that the available information fails to demonstrate an unmet health need that is not reasonably satisfied by Hopkins and Baxter."⁴⁹ Anticipating the disincentives that would be created if NIH initiated march-in proceedings, many universities opposed the petition, and NIH noted that to approve it would "have far-reaching repercussions on many companies' and investors' future willingness to invest in federally funded medical technologies."

- **Two petitions by Essential Innovations, Inc. (filed January 29, 2004; denied July 29, 2004) and by Knowledge Ecology International (KEI), the American Medical Students Association, the U.S. Public Interest Research Group, and the Universities Allied for Essential Medicines (filed October 25, 2012; denied November 1, 2013) calling for march-in with respect to certain patents owned and used by Abbott Laboratories (and subsequently, AbbVie) in the manufacture of the AIDS “booster” drug ritonavir (Norvir®), on the basis of excessive pricing.**

The 2004 petition requested march-in to “grant an open license to use six patents related to the manufacture of ritonavir. The grounds for the request are that the patent owner charges unreasonable prices for Norvir®/ritonavir, harming the public,”⁵⁰ highlighting a December 2003 400% price increase, and differential pricing between publicly funded and private sector health care plans (“As a consequence of the discriminatory price increase, US employers/insurers/consumers who buy ritonavir with private sector insurance will pay five to ten times more than employers/insurers/consumers in other high-income countries.”).

In denying the 2004 petition, NIH found that “No evidence has been presented that march-in could alleviate any health or safety needs that are not reasonably satisfied” and with regard to pricing, “because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by NIH, the NIH agrees with the public testimony that suggested that the extraordinary remedy of march-in is not an appropriate means of controlling prices.”⁵¹

NIH found that the 2012 petition made similar unsubstantiated claims as previously, namely that “AbbVie failed to achieve practical application of Norvir® because of its high, differential pricing structure between publicly funded and private sector health care plans.”⁵² The 2012 petition further requested NIH to adopt “two general policy rules regarding the commercialization of federally-funded inventions”⁵³ relating to allowable pricing disparities between the United States and other developed countries.

In denying the 2012 petition, NIH found that, "We do not think that the AbbVie pricing policies and pricing disparities between the United States and other countries trigger any of the four Bayh-Dole march-in criteria," and more generally, "NIH continues to agree with the public testimony in 2004 that the extraordinary remedy of march-in is not an appropriate means of controlling prices of drugs broadly available to physicians and patients."⁵⁴

► **Petition by Essential Inventions, Inc. requesting march-in for patents on Pfizer's glaucoma therapy latanoprost (Xalatan®), on the basis of pricing differentials between the U.S. and Canada and Europe (filed January 29, 2004; denied September 17, 2004)**

Petitioner stated, "(t)o remedy Pfizer's unreasonable pricing of Xalatan®, we request that you issue an "open license" for all latanoprost patents that are subject to federal rights,"⁵⁵ and "expressing concern that the price of Xalatan® is higher in the United States than in Canada or Europe."⁵⁶

NIH denied the petition, determining that, "Xalatan® has been available for use by glaucoma patients since 1996 and is being actively marketed by Pfizer and prescribed by physicians as both a first-line and second-line treatment. Accordingly, this drug has reached practical application and met health or safety needs as required by the Bayh-Dole Act."

As in its Norvir® denial, NIH noted that, "because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by the NIH, the NIH believes that the extraordinary remedy of march-in is not an appropriate means of controlling prices."⁵⁷

► **Petition by three individuals for march-in to relevant agalsidase beta (Fabrazyme®) patents in order to address shortages relating to manufacturing-related difficulties being monitored under a Genzyme Consent Decree with the FDA (filed August 2, 2010; denied December 1, 2010)**

Three individual patients with Fabry's disease petitioned HHS to grant "an open license under the Bayh-Dole Act that would allow supply of agalsidase beta in the U.S. and abroad to treat Fabry patients. Specifically, this petition requests that NIH authorize responsible entities and individuals to use U.S. Patent No. 5,356,804 and U.S. Patent No. 5,580,757 in order to manufacture, import, export or sell agalsidase beta,"⁵⁸ with the relevant patents being owned by Mount Sinai School of Medicine and exclusively licensed to Genzyme.

NIH denied the petition, determining that a march-in proceeding was not warranted because "any licensing plan that might result from such a proceeding would not, in our judgment, address the problem identified by the Requestors."⁵⁹

► **Petition filed by Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) to march-in to relevant patents on enzalutamide (Xtandi®) on the basis of high and/or differential pricing between the U.S. and other markets (filed January 4, 2016; denied June 20, 2016)**

Petitioners request the Department of Health and Human Services (DHHS), National Institutes of Health (NIH), and/or the Department of Defense (DoD) exercise a royalty-free right in the relevant patents awarded to the Regents of the University of California and licensed to Astellas Pharma, or to grant a request for march-in rights for the prostate cancer drug enzalutamide (Xtandi®), on the basis that the prices in the U.S. are higher than in other countries, despite U.S. taxpayer-funded grants from the NIH and DoD. More generally, petitioners request that the U.S. federal government "adopt the policy that the federal government will use its royalty-free rights, or grant licenses under federal march-in rights, when prices in the United States are excessive, and/or higher than they are in high income foreign countries, and to apply that policy in this case for patents on enzalutamide."⁶⁰

NIH denied the petition determining that a march-in proceeding was not warranted because the product had reached "practical application" in that it was "broadly available as a prescription drug."⁶¹

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from small businesses to all grantees, reported that some waivers were granted (implying that not all DoD-related patents should be removed from the calculation) GAO, 1987 at p. 17.

¹⁰ Report to Accompany H.R. 6933, 96th Cong., 2d Sess., H.Rept. 96-1307, Part 1, 3.

¹¹ 35 USC § 200–212.

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From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 3/14/2017 1:34:33 AM
To: Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] [/O=NIH/OU=NIEXCHANGE/cn=OD/cn=THALHAMC]
Subject: Re: Anyone have objection from KEI in 2017

Ok. Thanks

Sent from my iPhone

> On Mar 13, 2017, at 6:59 PM, Thalhammer-Reyero, Cristina (NIH/NHLBI) [E] <cristina.thalhammer-reyero@nih.gov> wrote:
>
> Jamie Love did not object to my license, just sent me a request for "a copy of the analysis done to address the requirements of 35 USC 209(a) and 35 USC 209(f). After my response he filed a FOIA request for the analysis and all correspondence with the company.
>
> Cristina
>
> Cristina Thalhammer-Reyero, Ph.D., M.B.A.
> Senior Licensing and Patenting Manager
> Office of Technology Transfer and Development
> National Heart, Lung and Blood Institute
> tel: : +1-301-435-4507
> ThalhamC@mail.nih.gov
>
> This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.
>
> -----Original Message-----
> From: Rohrbaugh, Mark (NIH/OD) [E]
> Sent: Monday, March 13, 2017 5:00 PM
> To: NIH TDC Long
> Subject: Anyone have objection from KEI in 2017
>
> From FR notice of intent to grant?
>
> Thx
> Mark
>
> Sent from my iPhone

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=591AB6B2424B4B8997082718CBB29FAB-ROHRBAUM]
Sent: 8/9/2017 1:42:20 PM
To: Gottesman, Michael (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=918c2344931542a592d00dbe83d3d5a3-gottesmm]
CC: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Burklow, John (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2e57f267323b43c08be856acb5b964ca-burklowj]; Rogers, Karen (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b23ef4ca2fa14a6eb174ee611953a396-rogersk]
Subject: Re: Salubris Biotherapeutics

This is a standard proposed licensing agreement that went through normal procedures. The article is very biased and stirred up by KEI Jamie Love. He regularly asks ICs for more information about the companies we are proposing to license, what are the terms, how did we justify an exclusive, have we included price controls, etc. ICs have been telling him this is business confidential information. Obviously, posting a notice in the fed reg seeking comment on the proposed license is not "quiet". The regs only require a 15 day posting and that is what OTT and now ICs have been doing routinely. I have asked for the internal memo that justifies the decision.

Sent from my iPhone

On Aug 9, 2017, at 8:39 AM, Gottesman, Michael (NIH/OD) [E] <GottesmM@mail.nih.gov> wrote:

I'll check it out.
Michael

From: Tabak, Lawrence (NIH/OD) [E]
Sent: Wednesday, August 9, 2017 8:10:02 AM
To: Gottesman, Michael (NIH/OD) [E]
Cc: Burklow, John (NIH/OD) [E]
Subject: Salubris Biotherapeutics

Michael,
Could you get me the background on this eclip:

THE U.S. IS QUIETLY GIVING A CHINESE BILLIONAIRE A MONOPOLY ON A NEW LIVER CANCER DRUG. The [Huffington Post](#) (8/8, Kaufman, 6.63M) reports the National Institutes of Health has proposed granting an exclusive license "for a new liver cancer drug" to Salubris Biotherapeutics Inc., which is the Maryland-based arm of the Chinese drug company Shenzhen Salubris Pharmaceuticals Co., Ltd. The article reports that "the proposal comes amid growing public backlash to deals that give pharmaceutical companies monopolies on drugs and vaccines developed through taxpayer-funded research without requiring them to sell the drugs back to Americans at a reasonable price."

Thanks
larry

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIH/OD/CN=ROHRBAUM]
Sent: 3/15/2016 7:13:45 PM
To: Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIH/OD/CN=NIAID/cn=MMOWATT]
Subject: Re: Comments from KEI

Are you available now. b6

Sent from my iPhone

On Mar 15, 2016, at 12:54 PM, Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov> wrote:

Hi Mark,

Following up on this, as it is rather urgent.

Are you available to chat (10 minutes max, I think) later today?

I can be available after 2:30, except for 4-5.

Thanks,

Mike

From: Mowatt, Michael (NIH/NIAID) [E]
Sent: Monday, March 14, 2016 4:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>
Subject: Comments from KEI

Hi Mark,

Thanks for speaking with Rick Williams about the comments we received from J Love in response to our recent FRN regarding an exclusive license.

Dale Berkley suggested b5 Can you spare a few minutes tomorrow to discuss?

Let me know what works for you.

Thanks,

Mike

Michael R. Mowatt, Ph.D.

Director, Technology Transfer and Intellectual Property Office

National Institute of Allergy and Infectious Diseases

National Institutes of Health

U.S. Department of Health and Human Services

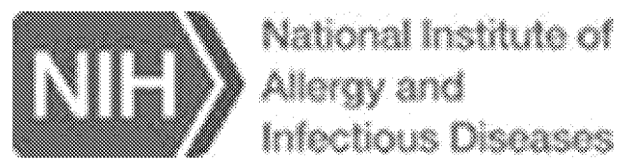
<http://www.niaid.nih.gov/labsandresources/techdev/Pages/default.aspx>

+1 301 496 2644

<image001.jpg>

REL0000024815

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From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 3/13/2017 10:44:38 PM
To: Lambertson, David (NIH/NCI) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=lambertsond]
Subject: Re: Anyone have objection from KEI in 2017

Thx

Sent from my iPhone

> On Mar 13, 2017, at 6:12 PM, Lambertson, David (NIH/NCI) [E] <david.lambertson@nih.gov> wrote:
>
> I have not had any so far.
>
> David A. Lambertson, Ph.D.
> Senior Technology Transfer Manager
> Technology Transfer Center
> National Cancer Institute/NIH
> david.lambertson@nih.gov
> <http://ttc.nci.nih.gov/>
>
> 9609 Medical Center Drive, Rm 1-E530 MSC 9702
> Bethesda, MD 20892-9702 (USPS)
> Rockville, MD 20850-9702 (overnight/express mail)
> Phone (Main Office): 240-276-5530
> Phone (direct): (240) 276-6467
> Fax: 240-276-5504
>
> Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents
>
> -----Original Message-----
> From: Rohrbaugh, Mark (NIH/OD) [E]
> Sent: Monday, March 13, 2017 5:00 PM
> To: NIH TDC Long <niaaatdcl-l@mail.nih.gov>
> Subject: Anyone have objection from KEI in 2017
>
> From FR notice of intent to grant?
>
> Thx
> Mark
>
> Sent from my iPhone

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 3/13/2017 10:44:23 PM
To: Knabb, Jim (NIH/NCI) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Knabbjr73e]
Subject: Re: Anyone have objection from KEI in 2017

Thx. Good to know

Sent from my iPhone

> On Mar 13, 2017, at 5:27 PM, Knabb, Jim (NIH/NCI) [E] <jim.knabb@nih.gov> wrote:
>
> Hi Mark,
>
> My FR notice just expired and I did not receive an objection from KEI.
>
> This isn't exactly what you were looking for but thought I'd share from a n-number perspective.
>
> Hope you are well.
> Jim
>
> -----Original Message-----
> From: Rohrbaugh, Mark (NIH/OD) [E]
> Sent: Monday, March 13, 2017 5:00 PM
> To: NIH TDC Long <n1aaatdc1-1@mail.nih.gov>
> Subject: Anyone have objection from KEI in 2017
>
> From FR notice of intent to grant?
>
> Thx
> Mark
>
> Sent from my iPhone

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 3/22/2016 1:28:29 AM
To: Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=culhane]; Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Damianold]
Subject: Fwd: march in letter
Attachments: 1 Letter from 11 NGOs calling for NIH to take action on high drug prices.msg; ATT00001.htm

Sent from my iPhone

Begin forwarded message:

From: "Hudson, Kathy (NIH/OD) [E]" <Kathy.Hudson@nih.gov>
Date: March 21, 2016 at 9:09:03 PM EDT
To: "Wolinetz, Carrie (NIH/OD) [E]" <carrie.wolinetz@nih.gov>, "Hammersla, Ann (NIH/OD) [E]" <hammerslaa@mail.nih.gov>, "Hallett, Adrienne (NIH/OD) [E]" <adrienne.hallett@nih.gov>, "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>, "Jorgenson, Lyric (NIH/OD) [E]" <jorgensonla@od.nih.gov>, "Baker, Rebecca (NIH/OD) [E]" <bakerrg@od.nih.gov>
Subject: march in letter

Fyi attached.

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 1/12/2020 3:23:23 PM
To: Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Goldstein, Bruce (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb67e8fe5aa2452a8a7f200e5fb4335b-goldsteb]
Subject: FW: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder
Attachments: 1.10.2020 KEI Comments, Prospective Grant of Exclusive Patent License, Gene Therapy for Ocular Disease.pdf; Attachment A.pdf; Attachment B.pdf; Attachment C.pdf; NIHtoKEI re OcQuila 6Jan2020.docx

Mark, Dale, and Bruce—KEI's comments regarding our FR notice for OcQuila enclosed and my proposed response. Please comment.
I'd appreciate feedback before next Friday as I'd like to send a response letter back to them COB Jan 17, 2020.

Thanks!

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@nih.gov

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From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Friday, January 10, 2020 11:09 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder

Dear Mr. Shmilovich:

Attached, please find KEI's comments regarding "Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder" (84 FR 65169) and the relevant attachments.

Thank you,

Kathryn Ardizzone, Esq.
Counsel
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009

REL0000024851

kathryn.ardizzone@keionline.org
(202) 332-2670



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January 10, 2020

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
31 Center Drive Room 4A29
Bethesda, MD 20892
Via Email: Shmilovm@mail.nih.gov

Re: "Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disease"

Dear Mr. Shmilovich:

Knowledge Ecology International (KEI) is writing to comment on the "Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disease" to OcQuila Therapeutics, Ltd., as described in the Federal Register (FR) notice 84 FR 65169.¹ The license involves an adeno-associated virus (AAV) gene therapy that was tested in nine subjects in a single-site, Phase I/II, NIH-sponsored clinical trial that began in early 2015.

KEI supports the NIH's efforts to secure a commercial partner to develop the technology, which targets a disorder for which no FDA-approved treatment exists.² However, the terms of the license must reflect the value of the invention. Given its relatively advanced research and development stage, the regulatory incentives the licensee is likely to receive, the government's investment in the technology, and the price that OcQuila likely will be able to charge for the treatment, the NIH should negotiate a license with terms that are favorable to the public.

Unfortunately, the NIH's statements about the license indicate that it plans to grant exclusive, life-of-patent rights to the invention without accounting for its unique investment value.

¹

<https://www.federalregister.gov/documents/2019/11/26/2019-25685/prospective-grant-of-an-exclusive-patent-license-gene-therapy-for-ocular-disease>.

² <https://www.ott.nih.gov/technology/e-284-2012>.

Background

The proposed license covers an NIH invention described in two abstracts: E-284-2012, “Methods And Compositions For Treating Genetically Linked Diseases Of The Eye”³ and E-164-2018, “Newly Improved Method and Composition for Treating Genetically Linked Diseases of the Eye.”⁴

The invention is an AAV gene therapy, AAV8-scRS/IRBPhRS (hereinafter, “AAV-RS1”), which may offer a cure for x-linked juvenile retinoschisis (XLRS), a genetic disease that leads to juvenile macular degeneration and affects 1:15,000 males in the United States.⁵

The second abstract, E-164-2018, describes the use of an electric current to improve the efficacy of AAV-RS1. It characterizes the invention as a “[p]otentially curative therapy for XLRS, retinoschisis, age-related macular degeneration, diabetic retinopathy, Leber congenital amaurosis, retinal detachment, cysts, cystoid, macular edema, retinitis pigmentosa, and senile schisis.”⁶

According to the Notice, the prospective licensee, OcQuila Therapeutics, is incorporated in Delaware and the UK.

Discussion

1. The NIH has not demonstrated that it properly evaluated the necessity of granting an exclusive license or that it has ensured that the scope of rights will not be broader than reasonably necessary to induce the investment needed to commercialize the subject technology.

The NIH may not license an invention on an exclusive basis unless, among other conditions:

(1) “granting the license is a reasonable and necessary incentive to -- (A) call forth the investment capital and expenditures needed to bring the invention to practical application; or (B) otherwise promote the invention’s utilization by the public;” and

(2) “the [NIH] finds that the public will be served by the granting of the license ... and that the proposed scope of exclusivity is not greater than reasonably necessary[.]”

³ <https://www.ott.nih.gov/technology/e-284-2012>.

⁴ <https://www.ott.nih.gov/technology/e-164-2018>.

⁵ <https://www.ott.nih.gov/technology/e-284-2012>.

⁶ <https://www.ott.nih.gov/technology/e-164-2018>.

35 U.S.C. § 209(a)(1)-(2).

As explained below, KEI is concerned that the license does not satisfy these criteria. Rather than engaging in a fact-specific inquiry to determine the necessary incentive, the NIH appears to have assumed that an exclusive license for life of patent is appropriate because the subject invention is an “early-stage” gene therapy.

(a) Determining the necessary incentive requires a fact-specific analysis of the factors that influence a biomedical invention’s commercial potential.

Determining the incentive necessary for bringing a federally-owned invention to practical application is a fact-specific inquiry: As the NIH has acknowledged, “[t]he value of patent commercialization licenses are **not uniform** and **depend on many factors**[.]”⁷

The factors that influence pharmaceutical investment decisions include:

- The potential market size of the drug or biologic;
- “Existing incentives, such as the Orphan Drug Act, and fast track FDA review that affect how quickly the drug can be brought to market and offer financial incentives”;
- Clinical trial costs; and
- “Projected manufacturing costs upon FDA approval[.]”⁸

Another important factor influencing the value of a biomedical invention is its stage of research and development. As Dr. Mark Rohrbaugh⁹ testified to Congress, “[t]he closer a technology is to the marketplace, the lower the risk and cost to the licensee, and the more valuable the technology[.]”¹⁰

Below is a detailed discussion of how some of the relevant factors bear on the subject invention’s commercial value.

Research and Development Stage

As the NIH concedes, to determine the value of a patent license, the NIH must consider “the state of development” of the subject invention.¹¹

⁷ Attachment A (emphasis added).

⁸ Aylin Sertkaya et al., U.S. Dept. of Health & Hum. Serv., *Examination of Clinical Trial Costs and Carriers for Drug Development* (2014), <https://aspe.hhs.gov/report/examination-clinical-trial-costs-and-barriers-drug-development>.

⁹ Special Advisor for Technology Transfer to the NIH Deputy Director for Intramural Research.

¹⁰ Mark L. Rohrbaugh, *NIH: Moving Research from the Bench to the Bedside, Testimony before the House Committee on Energy and Commerce, Subcommittee on Health*, July 10, 2003, available at <https://www.govinfo.gov/content/pkg/CHRG-108hhrg88429/html/CHRG-108hhrg88429.htm>.

¹¹ Attachment A.

Development of new drugs and cell or gene therapies consist of four main stages -- discovery, preclinical testing, clinical trials involving human subjects, and the regulatory review by the FDA and other government regulators.¹² An invention's risk of failure varies widely based on its development stage.

AAV-RS1 has advanced to the third of the four development stages - clinical testing involving human subjects. It is being investigated in a single-site, Phase I/IIa clinical trial (NCT02317887) that started in February of 2015, after the NIH submitted, and the FDA approved, an IND application showing positive results from preclinical studies in rabbits¹³ and mice.¹⁴ Preliminary results from the human subject clinical trial indicate that the therapy is generally well tolerated.¹⁵

In assessing the terms and need for exclusivity in this license, the NIH has not accurately accounted for the invention's development stage.

KEI asked Mr. Shmilovich, the point of contact for the license, how the NIH is "negotiating this license in a way that reflects th[e] commercial potential of [AAV-RS1]."¹⁶

He responded:

The present invention is early stage The question has also been previously answered in Dr. Rohrbaugh's November 26, 2019 letter (enclosed), and the answer in that letter applies to the current case as well.¹⁷

There are two problems with this answer.

First, it mischaracterizes the invention's development stage. According to some widely quoted estimates, drug development takes, on average, fifteen years from start to finish,

¹² U.S. Gov't Accountability Office, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts* (2006), <https://www.gao.gov/assets/260/253726.pdf>.

¹³ Marangoni, Dario et al., *Preclinical safety evaluation of a recombinant AAV8 vector for X-linked retinoschisis after intravitreal administration in rabbits*, Human gene therapy. Clinical development vol. 25,4 (2014): 202-11. doi:10.1089/humc.2014.067.

¹⁴ Bush, Ronald A et al., *Preclinical Dose-Escalation Study of Intravitreal AAV-RS1 Gene Therapy in a Mouse Model of X-linked Retinoschisis: Dose-Dependent Expression and Improved Retinal Structure and Function*, Human gene therapy vol. 27,5 (2016): 376-89. doi:10.1089/hum.2015.142.

¹⁵ Catherine Cukra et al., *Retinal AAV8-RS1 Gene Therapy for X-Linked Retinoschisis: Initial Findings from a Phase I/IIa Trial by Intravitreal Delivery*, <https://doi.org/10.1016/j.ymthe.2018.05.025>.

¹⁶ Attachment A.

¹⁷ *Id.*

with basic discovery and preclinical testing lasting six and one half years, clinical trials taking seven years, and FDA approval lasting one and a half years.¹⁸

While there are fewer estimates of the time periods associated with the development of gene therapies, the estimates for drug development are at least a useful proxy for evaluating the assertion that a technology is at an “early stage.”

AAV-RS1 began clinical research involving human subjects -- the third of the four development stages -- five years ago.

There is evidence that FDA approval periods for a gene therapy may be shorter than approval periods for drugs.

The BLA for Luxturna, a gene therapy for blindness, was filed on May 16, 2017, and the FDA approval was given on December 19, 2017, just seven months later. The BLA for Zolgensma, a gene therapy for spinal muscular atrophy, was filed October 1, 2018, and FDA approval was granted on May 24, 2019, less than eight months later.

It is also useful to note that Novartis spend \$8.7 billion to acquire AveXis, which was the owner of Zolgensma, on April 9, 2018, nearly six months before the Zolgensma BLA was even filed.

We do not consider it reasonable to describe a gene therapy in clinical trials as “early stage,” although that may describe other indications including “schisis cavity associated ocular disease or injury” which is among the fields of use in the license.

The November 26 letter pertains to two other licenses/inventions, which were in the discovery and preclinical stages of development at the time of notice and comment, and thus, were not comparable to a technology in clinical testing involving human subjects.

The November 26 letter is the NIH’s response to two appeals to exclusive patent licenses. The first license pertained to a CAR T-cell therapy whose development stage was described as “**Discovery (Lead Identification)**” by the NIH in the relevant abstract.¹⁹ The second involved a gene therapy that was described as “preclinical” by the NIH Office of Technology Transfer (OTT) officer designated to answer questions about the license.

It is inconsistent with the Bayh-Dole Act requirement “that the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing

¹⁸ U.S. Gov’t Accountability Office, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts* (2006), <https://www.gao.gov/assets/260/253726.pdf>.

¹⁹ <https://www.ott.nih.gov/technology/e-205-2018> (emphasis added).

the invention to practical application” for the NIH to lump an invention that has performed successfully in a clinical trial into the same category as technologies that are still in the discovery or preclinical stages of development, and to treat those inventions the same when determining the necessary incentive and negotiating license terms.

The table below demonstrates how the NIH negotiates the same patent terms for inventions that vary in terms of development phase.

Table 1 - Cell or Gene Therapy NIH Patent License Comparison

Proposed License(s)	Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20 (84 FR 33270) and Autologus Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20 (84 FR 33272).	Genetically-Modified Lymphocytes for Cancer Therapy (84 FR 45503)	Gene Therapy for Ocular Disease (84 FR 65169)
Licensee	Kite Pharma	Intima Bioscience	OcQuila Therapeutics
Development stage, at time of notice and comment	Discovery (lead identification)	Preclinical	Phase I/II clinical trial started in February of 2015.
License terms	Exclusive, life of patent, worldwide ²⁰	Exclusive, life of patent, worldwide	Exclusive, life of patent, worldwide

Regulatory Incentives

Another factor relevant to an invention’s commercial value is the availability of regulatory incentives that provide additional market exclusivities, expedited FDA review, and valuable financial benefits.

As the NIH has noted, XLR5 is an orphan disease and thus will receive Orphan Drug designation, a regulatory incentive that confers seven years’ Orphan Drug market exclusivity and a twenty-five percent credit toward R&D costs,²¹ as well as other benefits such as 12 years of exclusive rights in regulatory test data.

²⁰ Although the NIH would not confirm the terms of these patent licenses, based on Dr. Rohrbaugh’s statements that the NIH typically negotiates licenses for life of patent, and that no pharmaceutical company would invest in developing a gene therapy without full exclusivity for life of patent, it can safely be inferred that these licenses in cell and gene therapies were exclusive, with worldwide rights, for life of patent.

²¹ 26 U.S.C. § 45C.

In addition, therapeutics such as AAV-RS1 that treat rare diseases or satisfy an unmet medical need qualify for expedited review programs such the FDA's fast-track,²² breakthrough therapy,²³ accelerated approval,²⁴ and priority review designation,²⁵ reducing the time and thus expense of further drug development and increasing the time that the sponsor may claim exclusive marketing rights in the invention.²⁶ Finally, because XLRS is a serious,²⁷ rare disorder that occurs in children, the invention's sponsor likely will receive a priority review voucher, a financial incentive likely worth roughly \$100 million, based upon recent sales of PRVs.²⁸

Depending on the costs of any necessary further drug development, these incentives may enable the NIH to secure a qualified commercial partner without granting exclusive, worldwide rights for life of patent in the invention.

Government Investment in the Technology

Dr. Rohrbaugh has characterized the NIH as being "like any other licensor of technology,"²⁹ when it grants exclusive patent licenses but that is not an accurate statement.

Unlike private-sector licensors, the NIH allocates millions of taxpayers' dollars toward the research and development costs of the inventions it seeks to license. The NIH does not appear to maximize its income from the licensing of NIH or NIH funded technologies. Indeed, according to the NIH technology transfer office, the total annual revenues from patent licenses in fiscal year 2018³⁰ were less than \$111 million. This can be compared to the \$176 million AveXis paid in 2018 for use of the patents on Zolgensma, a single gene therapy, before Zogensma was approved by the FDA.

The government's investment in a technology is a key factor that bears on the appropriate terms of its patent licenses, as recognized by 35 U.S.C. § 209(a).

²² 21 U.S.C. § 356(b).

²³ 21 U.S.C. § 356(a).

²⁴ 21 U.S.C. § 356(c).

²⁵ 21 U.S.C. § 360ff.

²⁶ Food & Drug Admin., *For Industry, Developing Products for Rare Diseases & Conditions*, <https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesCondit/default.htm> [<https://perma.cc/NX5L-CJQW>].

²⁷ According to the OTT, "XLRS causes progressive vision loss, and affected individuals are unable to perform simple daily activities such as reading, writing and driving. This condition can lead to vitreous hemorrhage and retinal detachment in up to 40% of patients – resulting in total blindness." <https://www.ott.nih.gov/technology/e-164-2018>.

²⁸ The average sale price for priority review vouchers approved thus far (for which information is publicly available) is at least \$144 million. Table 2, Oulu Wang, *Buying and Selling Prioritized Regulatory Review: The Market for Priority Review Vouchers As Quasi-Intellectual Property*, 73 Food & Drug L.J. 383 (2018); Selina McKee, *GW Sells Priority Review Voucher for \$105m*, Pharma Times, March 18, 2019, [http://www.pharmatimes.com/news/gw_sells_priority_review_voucher_for_\\$105m_1281953](http://www.pharmatimes.com/news/gw_sells_priority_review_voucher_for_$105m_1281953)

²⁹ Attachment B.

³⁰ <https://www.ott.nih.gov/reportsstats/ott-statistics>

The NIH has directed millions of dollars toward developing AAV-RS1.

At least two intramural research grants supported the invention. An article describing NCT02317887, titled “Retinal AAV8-RS1 Gene Therapy for X-Linked Retinoschisis: Initial Findings from a Phase I/IIa Trial by Intravitreal Delivery,” states that “[t]he Phase I/IIa trial and clinical assays” were supported by Project No. 1ZIADC000065,³¹ an NIH grant titled “Preclinical and Clinical Development of Treatment for X-Linked Retinoschisis.” According to RePORTER, 1ZIADC000065 has cost nearly \$7 million to date.

The second intramural research grant associated with the invention, Project No. 1ZIADC000077, is titled “Pathophysiology and Treatment of Retinal Degenerations in Animal Models.” The Principal Investigator for the project is Paul Sieving, former director of the NEI and one of the inventors of AAV-RS1.³² The abstract for the project describes preclinical testing of various methods of delivery of an AAV gene therapy to treat XLRS. The “Results” tab for the project lists some of the same scientific articles that the NIH has attributed to the licensed inventions. Funding to date has totalled over \$3.2 million.

Additional R&D Required to Bring Invention to Market

The next factor relevant to the “necessary incentive” is the likely cost of any additional research and development required to bring a technology to practical application. This, too, varies from invention to invention.

Dr. Rohrbaugh’s November 26, 2019 letter states that full exclusivity is justified for “early-stage therapeutics” because their clinical trials cost hundreds of millions of dollars. KEI disputes this estimate, especially when it comes to cell and gene therapies, but even if it were correct, NIH patent licenses required individualized consideration. Clinical trial costs vary by size of the patient population, number of sites, disease indication, investigational product, and a variety of other factors.³³ The small patient enrollment of NCT02317887 -- a single-site trial consisting of 9 enrolled subjects -- indicates that additional clinical research costs for AAV-RS1 could be relatively low. By way of contrast, PhRMA, in describing the costs of research and development needed to bring a new drug to market, claimed that Phase I trials may involve up to 100 patients, Phase II

³¹ Catherine Cukra et al., *Retinal AAV8-RS1 Gene Therapy for X-Linked Retinoschisis: Initial Findings from a Phase I/IIa Trial by Intravitreal Delivery*, <https://doi.org/10.1016/j.ymthe.2018.05.025>.

³²

<http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=%2Fnetacgi%2Fsearch-bool.html&r=1&f=G&l=50&co1=AND&d=PTXT&s1=sieving.INNM.&OS=IN/sieving&RS=IN/sieving>.

³³ Aylin Sertkaya et al., U.S. Dept. of Health & Hum. Serv., *Examination of Clinical Trial Costs and Carriers for Drug Development* (2014), <https://aspe.hhs.gov/report/examination-clinical-trial-costs-and-barriers-drug-development>.

trials average 100 to 500 patients, and Phase III trials “may enroll 1,000 to 5,000 patients or more across numerous clinical trial sites around the world.”³⁴

Luxturna (voretigene neparvovec-rzyl), another vector-based gene therapy to treat an inherited eye disorder, provides a helpful reference point for estimating the enrollment size of any further clinical studies necessary to gain FDA approval of AAV-RS1. Luxturna was approved on the basis of a Phase I trial and Phase III trial, consisting of 12 and 31 subjects, respectively.³⁵

Any trials needed to secure regulatory approval of AAV-RS1 are highly unlikely to require enrolling hundreds or thousands of patients to obtain FDA approval, and such trials are also highly unlikely to cost “hundreds of millions of dollars” - an assumption upon which Dr. Rohrbaugh bases his licensing decisions for gene therapies such as the instant invention.

Potential Revenues

The license is an attractive investment because of the high prices that the licensee likely will be able to charge for the resultant product. AAV-RS1, if successful, will be the first therapy to treat XLRS, meaning that it will face no competition in that disease indication. Further, because AAV-RS1 treats a potentially debilitating condition, patients will tolerate higher prices. Finally, Luxturna’s price of \$425,000 per eye sets the stage for how similar gene therapies will be priced. AAV-RS1 may have an advantage over Luxturna in arguing for high reimbursements because it is administered intravitreally - a much less invasive method of administration to that of Luxturna, which is delivered subretinally.³⁶ It is safe to say that if it makes it to market (particularly under the current expected exclusive licensing terms), and if the NIH refuses to curb excessive prices, AAV-RS1 likely will command very high prices.

Other Factors

In addition to the factors discussed above, the License Opportunity notices for the invention list the following advantages:

- The use of a low-seroprevalence, non-pathogenic AAV8 vector favors efficacy in a high percentage of the patient population;
- The use of a tissue specific promoter limits non-specific gene expression;

³⁴ http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

³⁵ <https://www.fda.gov/media/110141/download>.

³⁶ Joan W. Miller et al., *Breaking and Sealing Barriers in Retinal Gene Therapy*, Molecular Therapy Vol. 26 No 9, <https://doi.org/10.1016/j.ymthe.2018.08.003>.

- Demonstrated GMP manufacturing process;³⁷ and
 - Elicits a minimal immune response since humans have a high preexisting immunity to AAV2.
- (b) The NIH's analysis of the proposed license does not satisfy 35 U.S.C. § 209(a)(1)-(2) because the NIH has not engaged in a fact-specific consideration of the factors relevant to the invention's investment value.

The NIH's statements about this license indicate that it has not performed the analysis mandated by Section 209 because it has not accounted for the factors that bear on the invention's commercial value.

KEI asked Mr. Shmilovich, the point of contact for the license, whether the NIH had conducted an economic analysis of what would be required to bring AAV-RS1 to practical application. He responded: "This is not required for a grant of an exclusive license."³⁸

Mr. Shmilovich's answer begged the question: If an economic analysis is not required for a grant of an exclusive license, then what analysis does 35 U.S.C. § 209(a)(1) require?

In a follow-up email, KEI asked what analysis, if any, the NIH had undertaken before deciding to license the invention on an exclusive basis. Mr. Shmilovich answered: "XLRS is a rare disease and information about its incidence is readily available."³⁹ By citing the disease's prevalence, Mr. Shmilovich implied that an exclusive license is necessary in this instance because the invention's small patient population makes it a less desirable investment.

As KEI has explained, however, the invention's indication in a rare pediatric disease also makes it eligible for valuable regulatory incentives, and there is plenty of readily available evidence that treatments for rare diseases also charge extraordinarily high prices, and can generate significant revenues. For example, consider this report on the \$3.4 billion in 2018 sales for Soliris:

Alexion Pharmaceuticals (\$ALXN) may not have a huge market for Soliris, but it does have a recipe for success: an essential treatment for a frightening rare disease and a very, very hefty price tag.

Soliris was originally developed as a treatment for the life-threatening blood disorder paroxysmal nocturnal hemoglobinuria, a disease that only affects about 8,000 Americans. But at up to \$400,000 per year, Soliris--recognized as the world's most expensive drug--doesn't have to reach many patients to hit the blockbuster threshold.⁴⁰

³⁷ Companies must adhere to the FDA's good manufacturing practices (GMP) regulations. http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

³⁸ Attachment A.

³⁹ *Id.*

⁴⁰ <https://www.fiercepharma.com/special-report/soliris>.

Mr. Shmilovich's statement also ignores the fact that the license has commercial applications in other disorders, some with much larger patient populations, such as age-related macular degeneration (affecting 30 million people worldwide), diabetic retinopathy (more than three million cases per year in the United States), Leber congenital amaurosis, retinal detachment, cysts, cystoid, macular edema, retinitis pigmentosa, and senile schisis,⁴¹ making the potential market size much larger.

In a follow-up email, KEI asked Mr. Shmilovich if the NIH had considered any factors other than the prevalence of XLRS when concluding that an exclusive license was justified, and why he had not acknowledged the invention's other potential commercial applications. In an email apparently not intended for KEI, Dr. Rohrbaugh advised Mr. Shmilovich not to respond, and he never did.⁴²

If the NIH's analysis started and ended with the fact that the invention treats an orphan disease, it does not satisfy Section 209.

Based on past statements of Dr. Rohrbaugh, the only other fact the NIH appears to have considered with respect to the prospective license is that it involves a gene therapy. This, too, would be insufficient to satisfy the Bayh-Dole Act.

The following statements from Dr. Rohrbaugh's November, 26, 2019 letter indicate that, as a general matter, the NIH automatically assumes that exclusive, life of patent licenses are always required for gene therapies:

- "[NIH] works in a market for these early-stage therapeutic technologies in which there is essentially no demand for nonexclusive licenses."⁴³
- "[C]ompanies and investors have choices as to which early stage technologies to develop and, in taking on this risk and committing to commercialization, require an exclusive license for the full patent term."⁴⁴

In failing to assess the commercial potential of the covered inventions on an individualized basis, the NIH has not satisfied Section 209(a)(1)-(2) of the Bayh-Dole Act for the instant license.

2. The NIH has not sought the antitrust advice of the U.S. Attorney General regarding the license, as it is required to do under 40 U.S.C. § 559.

⁴¹ <https://www.ott.nih.gov/technology/e-164-2018>.

⁴² Attachment C.

⁴³ Attachment B (emphasis added).

⁴⁴ *Id.*

We object to the license unless the NIH first obtains the antitrust advice of the United States Attorney General, who confirms that the license would not be anticompetitive.

Under the Federal Property and Administrative Services Act, 40 U.S.C. §§ 101 *et seq.*, “[a]n executive agency shall not dispose of property to a private interest until the agency has received the advice of the Attorney General on whether the disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law.” 40 U.S.C. § 559(b)(1).

This includes when the NIH proposes to grant an exclusive license in federally-owned technology. “Property” is defined at 40 U.S.C. § 102 to mean “any interest in property,” with certain exceptions that do not include patents. Similarly, Section 559 creates certain exceptions that do not include patents.

41 C.F.R. § 102-75.270 supports the notion that the term “property” in Section 559 includes intellectual property rights such as patents.

41 C.F.R. § 102-75.270 - Must antitrust laws be considered when disposing of property?

Yes, antitrust laws must be considered in any case in which there is contemplated a disposal to any private interest of -

- (a) Real and related personal property that has an estimated fair market value of \$3 million or more; or
- (b) Patents, processes, techniques, or inventions, irrespective of cost.

KEI asked Mr. Shmilovich whether the NIH requested the advice of the U.S. Attorney General concerning the license. He responded “not required.” In the past, the NIH has asserted its position with respect to 40 U.S.C. § 559 as follows:

“The statute you reference is directed to the disposal (assignment) of government property. It has little relevance to our patent licensing activities, which are principally governed by the Bayh-Dole Act and its regulations.”

The NIH’s interpretation of 40 U.S.C. § 559 is incorrect.

The Bayh-Dole Act expressly incorporates federal antitrust laws. 35 U.S.C. § 209(a)(4) allows a federal agency to grant an exclusive license only if the license “will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws.” 35 U.S.C. § 211 provides that “[n]othing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law[.]” The Bayh-Dole Act sets out the areas in which the statute “shall take precedence over any other Act

which would require a disposition of rights in subject inventions[,]” 35 U.S.C. § 210, and mentions 21 separate statutes, but not the FPASA.

Second, the term “disposal” is not a defined term under 40 U.S.C. § 102 of the FPASA, and is not limited to “assignment” or “sale.” In fact, there are many examples of regulations and laws that include licensing amongst dispositions, either explicitly or by implication.

If NIH grants a fully-exclusive license to a federally-owned invention for life of patent, and allows termination of the license only in narrow, vaguely-defined circumstances, then it is effectively disposing of a government property interest so as to trigger 40 U.S.C. § 559.

3. In the event that the NIH decides to grant the license over our objections, we recommend that the NIH includes a series of provisions designed to safeguard the public interest and ensure that the license implements the governing principles in the PHS Technology Transfer Manual.

In the event that the NIH proceeds with the license, KEI requests that it includes the following provisions to protect the public’s interest in the technology:

1. **Price discrimination.** Any medical technology using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard.
2. **Low and middle income countries.** The exclusive license should not extend to countries with a per capita income less than 30 percent of the United States, in order to ensure that the patents do not lead to restricted and unequal access in developing countries. If the NIH rejects this suggestion, it needs to provide something that will give effect to the policy objective in the “United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy,” which states the following: “PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries.”
3. **Global registration and affordability.** The license should require OcQuila Therapeutics to disclose the steps it will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.

4. **Medicines Patent Pool.** The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the medical technology from competitive suppliers, including technology transfer, in developing countries, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology.
5. **Years of exclusivity.** We propose the license reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddi case. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. For example, the period of exclusivity in the license could be reduced by one year for every \$500 million in global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 U.S.C. § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”
6. **Transparency of R&D outlays.** The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Conclusion

We support the NIH's efforts to license AAV-RS1 to a commercial partner who appears to be qualified to bring it to practical application.

Commercializing a truly innovative therapy that satisfies an unmet medical need is certainly a positive. It is far less positive if all U.S. taxpayers funded a substantial portion of the expense of developing the invention, and only a narrow segment of society likely will be able to afford it without facing financial hardship.

This outcome may be avoidable if the NIH does its job, and exercises the significant leverage it has to at least make reasonable efforts to negotiate favorable licensing terms, such as a co-exclusive license or shorter period of exclusivity. Such a course of action is not merely desirable, it is required.

Federal law dictates that before granting this license on an exclusive basis, the NIH must conduct the analysis required by 35 U.S.C. § 209(a)(1)-(2) and conclude that no qualified firm would develop the inventions without a fully-exclusive license for life of patent.

We believe this is unlikely. Far from being a gleam in the eye of an NIH scientist, AAV-RS1 has successfully completed the riskiest phases of drug development and part of a Phase I/II clinical trial, and that legwork was funded by the public. The license that the NIH negotiates must reflect the inventions' commercial value.

Sincerely,

Knowledge Ecology International



kathryn ardizzone <kathrynardizzonekei@gmail.com>

Questions regarding the proposed license to OcQuila Therapeutics, 84 FR 65169

Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>

Tue, Jan 7, 2020 at 8:56 AM

To: Kathryn Ardizzone <kathryn.ardizzone@keionline.org>, Luis Gil Abinader <luis.gil.abinader@keionline.org>, Jamie Love <james.love@keionline.org>, "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>, "Goldstein, Bruce (NIH/NHLBI) [E]" <goldsteb@mail.nih.gov>

Dear Ms. Ardizzone:

Regarding your email. Our responses are shown below in blue:

Dear Mr. Shmilovich:

Thank you for answering my colleague Luis Abinader's questions regarding the proposed license to OcQuila. I have a few questions about the licensed inventions.

1. The clinical trial NCT02317887, Study of RS1 Ocular Gene Transfer for X-linked Retinoschisis, investigated the first invention listed in the notice. **Will the second invention, Newly Improved Method and Composition for Treating Genetically Linked Diseases of the Eye, be investigated in any clinical trials, including NCT02317887?** So far, it appears that it has only been studied in mice, yet the development stage for the invention is listed as "clinical" in this licensing opportunity notice.

That is not known at this time and will be up to the licensee and NEI.

2. Can you provide us a copy of the unpublished patent applications associated with the second invention? This is not confidential business material and will help us to evaluate the license.

The PCT application has not yet published yet. Under our policy, until a PCT application is published, it is only available under a Confidential Disclosure Agreement.

3. You told Mr. Abinader that NIH is not required to perform an economic analysis to determine that an exclusive license is appropriate. **What analysis, if any, did you undergo before deciding to propose**

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an exclusive license? If you determined that exclusivity was necessary, on what basis did you so conclude?

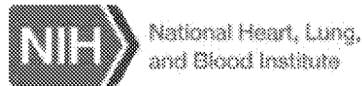
XLRS is a rare disease and information about its incidence is readily available.

4. Dr. Mark Rohrbaugh, Special Advisor for Technology Transfer to the NIH Deputy Director for Intramural Research, has publicly stated that “[t]he closer a technology is to the marketplace, the lower the risk and cost to the licensee, and the more valuable the technology from a royalty standpoint.” Mark L. Rohrbaugh, NIH: Moving Research from the Bench to the Bedside, Testimony before the House Committee on Energy and Commerce, Subcommittee on Health, July 10, 2003, <https://www.govinfo.gov/content/pkg/CHRG-108hhrg88429/html/CHRG-108hhrg88429.htm>. **How is the NIH negotiating this license in a way that reflects that commercial potential of these inventions? Are all inventions treated equally per NIH's licensing practices regardless of development stage, risk, and cost?**

The value of patent commercialization licenses are not uniform and depend on many factors including the state of development. The present invention is early stage. Negotiation of a license, including royalties, does not occur until a final decision is made based on any competing applications and comments submitted during the notice period. The question has also been previously answered in Dr. Rohrbaugh's November 26, 2019 letter (enclosed), and the answer in that letter applies to the current case as well.

Regards,

Michael A. Shmilovich, Esq., CLP




Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019

shmilovm@nih.gov

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 **KEI appeal response 11262019.pdf**
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kathryn ardizzone <kathrynardizzonekei@gmail.com>

Questions regarding the proposed license to OcQuila Therapeutics, 84 FR 65169

Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
To: kathryn ardizzone <kathryn.ardizzone@keionline.org>

Tue, Jan 7, 2020 at 10:38 AM

I suggest not answering

Sent from my iPhone

On Jan 7, 2020, at 10:35 AM, kathryn ardizzone <kathryn.ardizzone@keionline.org> wrote:

Dear Mr. Shmilovich:

Thank you for your prompt response.

I was hoping you could clarify your answers to Questions 3 and 4.

Question 3 asked how the NIH fulfilled its statutory mandate to determine that exclusivity was a necessary incentive. Your answer cited the target disease and its prevalence, which you state is available online. KEI has researched XLRs and is aware of its low prevalence. I understand your response to mean that NIH considered only those factors when deciding to grant exclusivity. **Please let me know if that understanding is incorrect and what, if any, other factors were considered.** Also, please note that the license as described in the FR is not limited to XLRs. The second invention covered by the license is described as "Potentially curative therapy for XLRs, **retinoschisis, age-related macular degeneration, diabetic retinopathy, Leber congenital amaurosis, retinal detachment, cysts, cystoid, macular edema, retinitis pigmentosa, and senile schisis**" and the field of use described in the FR is not limited to XLRs - it extends to "**schisis cavity associated ocular disease or injury.**" How does your answer account for the other disease indications?

Per Question 4, you referred KEI to Dr. Rohrbaugh's statements in his November 26, 2019 letter which refer to **two other licenses**. Please note that Question 4 is specific to the NIH's analysis of **this license**. Also, you call this technology "early stage." Please clarify how you define early stage. According to the PhRMA, typical drug development proceeds through four phases: (1) basic research, (2) preclinical trials, (3) clinical trials, and (4) FDA New Drug Application (NDA) filing and approval. As you know, this invention has proceeded past basic discovery and preclinical trials, and based on preclinical trial results, an IND was submitted and the invention proceeded to a **Phase I/IIa clinical trial** that has already reported some positive preliminary results. How does this meet the definition of early stage?

Finally, why is the analysis the same for this invention as those covered by the Nov. 26 letter? As far as I understand, the inventions discussed in the letter had not been investigated in human clinical trials at the time the license was noticed, so they had a different stage of development.

Thank you in advance for your consideration.

On Tue, Jan 7, 2020 at 8:58 AM Shmilovich, Michael (NIH/NHLBI) [E]
<michael.shmilovich@nih.gov> wrote:

Dear Ms. Ardizzone:

REL0000024851.0004

Regarding your email. Our responses are shown below in blue:

Dear Mr. Shmilovich:

Thank you for answering my colleague Luis Abinader's questions regarding the proposed license to OcQuila. I have a few questions about the licensed inventions.

1. The clinical trial NCT02317887, Study of RS1 Ocular Gene Transfer for X-linked Retinoschisis, investigated the first invention listed in the notice. **Will the second invention, Newly Improved Method and Composition for Treating Genetically Linked Diseases of the Eye, be investigated in any clinical trials, including NCT02317887?** So far, it appears that it has only been studied in mice, yet the development stage for the invention is listed as "clinical" in this licensing opportunity notice.

That is not known at this time and will be up to the licensee and NEI.

2. Can you provide us a copy of the unpublished patent applications associated with the second invention? This is not confidential business material and will help us to evaluate the license.

The PCT application has not yet published yet. Under our policy, until a PCT application is published, it is only available under a Confidential Disclosure Agreement.

3. You told Mr. Abinader that NIH is not required to perform an economic analysis to determine that an exclusive license is appropriate. **What analysis, if any, did you undergo before deciding to propose an exclusive license? If you determined that exclusivity was necessary, on what basis did you so conclude?**

XLRS is a rare disease and information about its incidence is readily available.

4. Dr. Mark Rohrbaugh, Special Advisor for Technology Transfer to the NIH Deputy Director for Intramural Research, has publicly stated that **"[t]he closer a technology is to the marketplace, the lower the risk and cost to the licensee, and the more valuable the technology from a royalty standpoint."** Mark L. Rohrbaugh, NIH: Moving Research from the Bench to the Bedside, Testimony before the House Committee on Energy and Commerce, Subcommittee on Health, July 10, 2003, <https://www.govinfo.gov/content/pkg/CHRG-108hhrg88429/html/CHRG-108hhrg88429.htm>. **How is the NIH negotiating this license in a way that reflects that commercial potential of these**

inventions? Are all inventions treated equally per NIH's licensing practices regardless of development stage, risk, and cost?

The value of patent commercialization licenses are not uniform and depend on many factors including the state of development. The present invention is early stage. Negotiation of a license, including royalties, does not occur until a final decision is made based on any competing applications and comments submitted during the notice period. The question has also been previously answered in Dr. Rohrbaugh's November 26, 2019 letter (enclosed), and the answer in that letter applies to the current case as well.

Regards,

Michael A. Shmilovich, Esq., CLP

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National Heart, Lung, and Blood Institute **image001.jpg**
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National Heart, Lung,
and Blood Institute

Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
Michael Shmilovich, Esq, CLP
shmilovm@mail.nih.gov

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 11/20/2018 8:19:06 PM
To: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"
Attachments: NIH Prospective License Ovensa type 2 diabetes, 20 November 2018.pdf

The Spreader of Love and I have been trading emails about this FR notice for the better part of a week.

b5

Thoughts?

From: James Love <james.love@keionline.org>
Sent: Tuesday, November 20, 2018 15:10
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Brook Baker <b.baker@northeastern.edu>; Alex Lawson <alawson@socialsecurityworks.org>; Allison Love <mardiniavon@hotmail.com>; Erin Little <erin.little@sucreblue.org>
Subject: Joint comments on "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)"

Dear Michael Shmilovich

Attached are the joint comments for the notice published in the Federal Register (83 FR 55556), "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)," concerning a prospective exclusive license to Ovensa, a firm located in Canada.

From:

Organizations

HealthGAP
Knowledge Ecology International (KEI)
Social Security Works (SSW)
The Young Professionals Chronic Disease Network (YP-CDN)

Individuals

Allison Love Mardini (type 2 diabetes patient)
Brook K Baker
James Love

--

James Love. Knowledge Ecology International
<http://www.keionline.org>
twitter.com/jamie_love

REL0000024854

November 20, 2018

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
31 Center Drive, Room 4A29, MSC2479
Bethesda, MD 20892-2479
shmilovm@mail.nih.gov

Dear Michael Shmilovich,

We are writing in regard to the notice published in the Federal Register ([83 FR 55556](#)), "Prospective Grant of Exclusive Patent License: Therapeutics for Insulin Resistance and Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NASH/NAFLD)," concerning a prospective exclusive license to [Ovensa](#), a firm located in Canada.

The patent rights include all continuing U.S. and foreign patents/patent applications thereof for the following inventions:

1. HHS Ref. No. E-103-2013-0, U.S. Provisional Patent Application 61/839,239, "Glucan-Encapsulated siRNA For Treating Type 2 Diabetes Mellitus," filed June 25, 2013,
2. International Patent Application [PCT/2014/043924](#) filed June 24, 2014,
3. European Patent Application [14818342.9](#) filed June 24, 2018, and
4. U.S. Patent [10,077,446](#) filed June 24, 2014 and issued September 18, 2018.

The license includes inventions relating to new methods of treating type 2 diabetes or preventing the progression of insulin resistance to overt diabetes.

According to the notice, the license will be "worldwide," and the license may or may not, "be limited to products sold that include therapeutic siRNAs encapsulated in nanoparticles made from either glucan based biopolymers and/or Ovensa's TRIOZANTM (N,N,N-Trimethyl Chitosan) proprietary biopolymer."

Ovensa appears to be a small company located in Ontario, Canada. The company LinkedIn profile lists 4 employees, of which not all appear to be working exclusively for the company. The page for "Management Team" on the Ovensa website lists two persons.

Diabetes is not a rare disease. According to the CDC, more than 30 million Americans have diabetes, and 90% to 95% of them have type 2 diabetes.¹

According to the IDF Diabetes Atlas Eighth Edition (published in 2017), approximately 425 million adults were living with diabetes; and by 2045, this will rise to 629 million.

¹ <https://www.cdc.gov/diabetes/basics/type2.html>

Also note that per the IDF Diabetes Atlas, 4 out of 5 persons living with diabetes live in low and middle income countries where access to new medicines is particularly limited due to unaffordable prices.

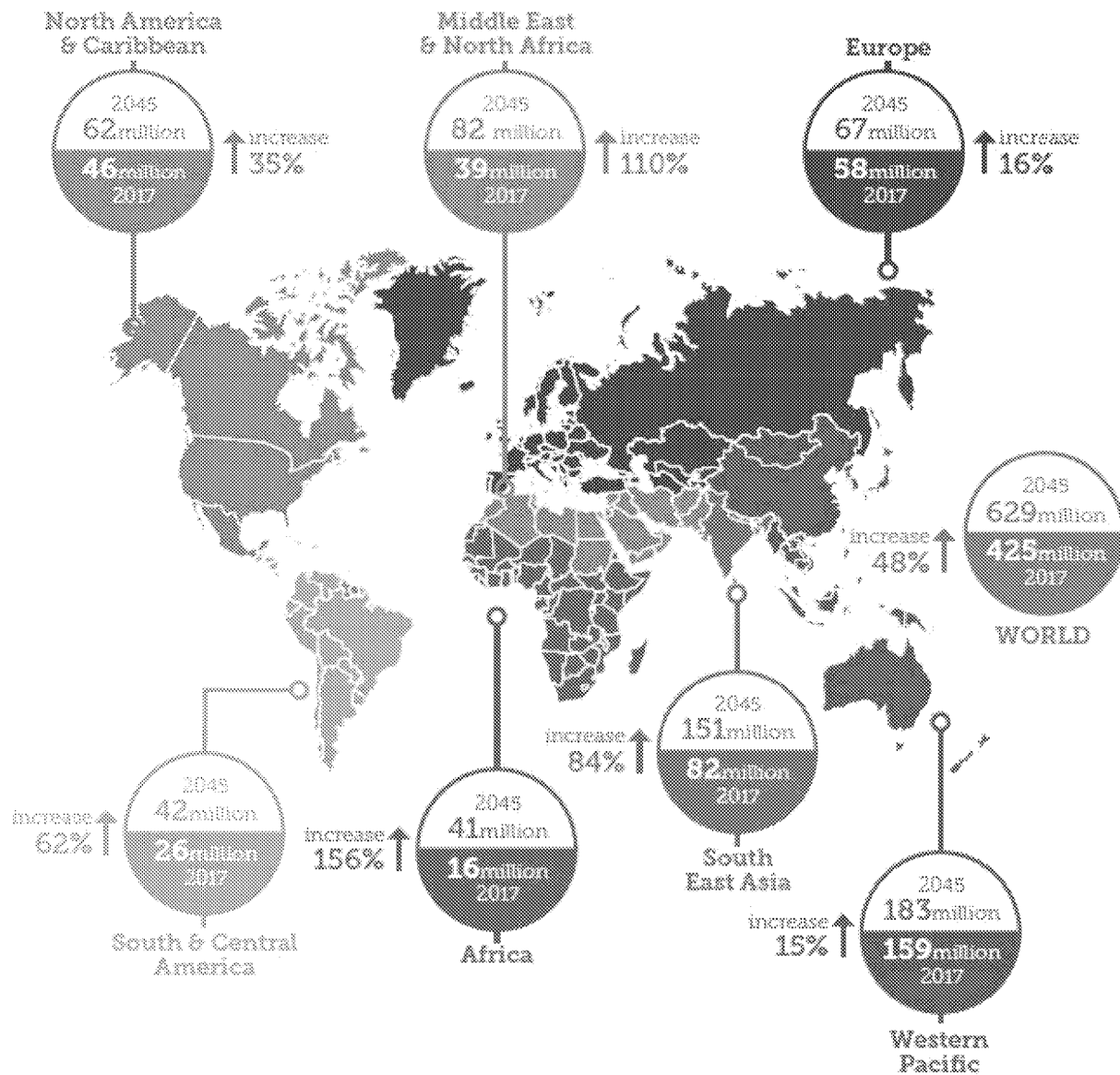


Figure source: IDF Diabetes Atlas Eighth Edition

The NIH has shared a press release published on Marketwatch.com, which provides the following estimates of the market for drugs to treat diabetes.²

“The global Antidiabetic Drug market is valued at 49600 million US\$ in 2017 and will reach 96700 million US\$ by the end of 2025, growing at a CAGR of 10.0% during 2018-2025.”

Cost of development

The NIH has indicated that the most recent \$1.38 million in company financing received by Ovensa³ is evidence that the company has sufficient resources to bring the invention to practical application. The NIH should take into account the relatively modest amount of resources necessary for development when evaluating the appropriate scope of rights for the license, including the term of exclusive rights.

40 USC § 599

At the appropriate time in the licensing process, we expect the NIH to obtain advice from the Attorney General (as is required under 40 USC § 599) to determine if the “disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law.”

The Bayh-Dole Act provides that “Nothing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law” [35 USC § 211 - Relationship to antitrust laws].

The Bayh-Dole Act sets out the areas where the Bayh-Dole Act “shall take precedence over any other Act which would require a disposition of rights in subject inventions” [35 USC § 210 - Precedence of chapter], and mentions 21 separate statutes, but does not include 40 USC § 599.

35 USC § 209

Assuming the NIH has conducted a proper analysis to determine if any exclusive rights are necessary to induce investments in research and development (R&D) to bring the inventions to practical application,⁴ we ask the NIH to limit the “proposed scope of exclusivity” so that it is “not

² Global Antidiabetic Drug Market 2018 Share, Trend, Segmentation and Forecast to 2025
June 28, 2018. Wise Guy Reports.

<https://www.marketwatch.com/press-release/global-antidiabetic-drug-market-2018-share-trend-segmentation-and-forecast-to-2025-2018-06-28>

³ http://ovensa.com/wp-content/uploads/2017/10/FINAL_Communique_OVENSA_ENG.pdf

⁴ 35 USC 201(f). The term “practical application” means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system;

greater than reasonably necessary to provide the incentive for bringing the invention to practical application,” as is required by 35 USC § 209.

Such an analysis should include an estimate of the expected costs (adjusted for risks and the costs of capital) to bring the invention to practical application, as well as reasonable estimates of the revenue from the sale of the drug or other technology that would be necessary as an adequate incentive for that investment. If the expected investments are small (which seems to be the case given the modest financial resources of Ovensa) and the diabetes market is large, as the NIH suggested with reference to the Wise Guy Reports estimate, then the NIH should limit either (1) the number of years of exclusivity (2) the prices that can be charged, (3) the maximum revenue before exclusivity is reduced or eliminated, or (4) some combination of 1-3.

35 USC § 201(f) - definition of practical application

The Bayh-Dole defines certain terms in 35 USC § 201, including the term “practical application.”

(f) The term “practical application” means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms. [emphasis added]

“Available to the public” and “reasonable terms” taken together include the price to the public being reasonable. For the public, the price is the primary term of the transaction.

Proposals for safeguards to protect the public’s rights in the patented inventions

We propose the following measures to protect the public’s interest in any license to the Canadian firm, Ovensa.

1. No discrimination against U.S. residents in pricing

We ask that the NIH include language in the proposed exclusive license to ensure that the prices in the U.S. for any drug, vaccine, medical device or other health technology using the inventions are not higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or government regulations available to the public on reasonable terms.

We consider this a modest and indeed minimalist request to protect U.S. residents, who paid for the R&D that created the licensed inventions.

2. Additional provisions on affordability

The NIH should require that prices for products in the United States that use the NIH-owned patented inventions do not exceed the estimated value of the treatment, as determined by independent health technology assessments selected by HHS.

The NIH should also create an obligation to set prices low enough that patient co-payments under third party Medicare programs are affordable.

3. Reduce term of exclusivity when revenues are large

In addition to an external reference pricing test, we propose that the exclusivity of the license in the U.S. should be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks.

Given the modest cost of acquiring an NIH-patented invention, the amount of money the developer needs in sales to justify additional investments in R&D is reduced, as compared to cases where a company develops or acquires the technology from non government sources.

This request is consistent with the statutory requirements of 35 USC § 209, which demands that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”

One possible implementation of revenue benchmarks is as follows: exclusivity will be reduced by one year for every \$500 million in revenue equivalents, earned after the first \$1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. However, the NIH could choose different benchmarks, so long as the limits on exclusivity address the requirements of 35 USC § 209, in that the incentive is “not greater than reasonably necessary.”

4. Low and Middle Income Countries

In general, we are concerned that several NIH-funded inventions are not accessible in low and middle income countries, due to prices that are high and not affordable in markets where per capita incomes are significantly lower than the United States. For this reason, we generally ask, and are asking in this specific case, that the NIH limit the exclusivity in the license to countries that have per capita incomes that are at least 30 percent of the United States.

We also generally ask the NIH to reach out to the Medicines Patent Pool (MPP), in order to enter into an agreement that gives the MPP an option to negotiate non-exclusive open licenses for the inventions in developing countries.

According to the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy:"

"PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

For this license, we ask that the NIH clarify the geographic area of the license, and provide information on the measures that will be taken to ensure the policy of "broad accessibility for developing countries" is actually implemented.

The policy of promoting access seems to have been routinely ignored in the past. The NIH has rejected efforts to restrict the geographic area of exclusive rights or to impose access requirements on companies holding licenses, including in cases involving firms with deplorable records of price gouging worldwide.

We also ask the PHS to reconsider the use of the term "developing countries," which is no longer the most useful way to describe a category of countries for which access is a challenge.

There is no consensus on how to define "developing countries." The WTO allows its members to self identify as "developing."⁵

Policy makers often prefer to use the term "low and middle income countries" (LMIC), but this also requires a thoughtful definition.

The World Bank publishes and updates a list of country classifications every year, but the World Bank definition is anchored in a methodology from the 1980s that was based in part upon the cost of buying food, a poor proxy for global wellbeing today.

The World Bank definition of "high income" was adopted in 1989 by the Bank's Executive Directors on the basis of a staff report on per capita income measures. The high income threshold was determined by an "explicit benchmark of \$6,000 per capita in 1987 prices," and updated annual with an adjustment for inflation.⁶ With real growth in per capita incomes, the number of countries that qualify as high income has continued to rise, and at some point, most countries will probably qualify.

⁵ https://www.wto.org/english/tratop_e/devel_e/d1who_e.htm

⁶ Per Capita Income: Estimating Internationally Comparable Numbers, Board Report 79541, January 13, 1989. International Economics Department.

Our recommendation for the NIH is to consider relative per capita income as a useful starting metric for policies designed to mitigate inequality of access, recognizing that in some cases other factors such as prevalence of a disease may be appropriate to consider.

The PCT application referenced in the Federal Register notice identified a very large number of designated countries for foreign patent applications, including the African Regional Intellectual Property Organization (ARIPO), the African Intellectual Property Organization (AIPO), and low income countries in Eastern Europe, Asia, South America and the Caribbean.

Designated AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, States: CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
African Regional Intellectual Property Organization (ARIPO) (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW)
Eurasian Patent Office (AM, AZ, BY, KG, KZ, RU, TJ, TM)
European Patent Office (EPO) (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR)
African Intellectual Property Organization (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)

The WIPO PCT web page for this application notes that after the 30 month period following the priority date, the NIH has only pursued patents at the European Patent Organization and the U.S. PTO, a fact confirmed today by the NIH.

Our concerns about access outside the United States are therefore focused in part on the EPO member states that have per capita incomes significantly lower than the United States.

In 2017, the United States per capita income was estimated by the World Bank to be \$58,270. Thirty percent of this figure is \$17,481.

We are specifically asking the NIH to exclude from the geographic area of any exclusive right, the following EPO member states, based upon the fact that their 2017 per capita income was less than 30 percent of U.S. per capita income.

Table 1: EPO members, less than 30 percent 2017 U.S. per capita income

1. Albania,	\$ 4,320
2. Bulgaria	\$ 7,760
3. Croatia	\$12,430
4. Hungary	\$12,870

5. Lithuania	\$15,200
6. Latvia	\$14,740
7. Macedonia	\$ 4,880
8. Poland	\$12,710
9. Romania	\$ 9,970
10. Serbia	\$ 5,180
11. Slovenia	\$16,610
12. Turkey	\$10,930

Test data

In addition, we ask the NIH to include provisions that would require the licensed patent holders to waive any exclusive rights regard test data and any patent-registration linkage rights that may exist in any country with a per capita income less than 30 percent of U.S. per capita income.

This is important because a number of trade agreements and bilateral pressures force low and middle income countries to enact laws granting exclusive rights in test data, in most cases, without the possibility of exceptions, even in cases involving excessive prices.

A provision waving exclusive rights in test data in countries with lower incomes is necessary for the NIH to implement of the PHS policy "to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

5. Transparency

The licensee should be required to file an annual report to the NIH on the research and development costs associated with the development of any product that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 USC § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

Sincerely,

Organizations

HealthGAP

Knowledge Ecology International (KEI)

Social Security Works (SSW)

The Young Professionals Chronic Disease Network (YP-CDN)

Individuals

Allison Love Mardini (type 2 diabetes patient)

Brook K Baker

James Love

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 3/21/2016 11:14:35 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: March in Petition
Attachments: Xtandi-March-In-Request-Letter-14Jan2016(5).pdf

Mark: The following is Kathy's email to the Army. I thought she also mentioned she would follow-up.

From: Hudson, Kathy (NIH/OD) [E]
Sent: Monday, February 29, 2016 11:53 AM
To: 'Jonathan.woodson@ha.osd.mil' <Jonathan.woodson@ha.osd.mil>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>; Lauer, Michael (NIH/OD) [E] <Michael.Lauer@nih.gov>; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Muroff, Julie (NIH/OD) [E] <muroffj@od.nih.gov>
Subject: March in Petition

Dear Dr. Woodson,

It was great to see you at the PMI event last week; what an amazing day.

I mentioned to you that we have received a march in request related to a prostate cancer drug that was developed with NIH and Army supported research. We understand that Dr. Elizabeth Arwine from the US Army MedCom USAMMRC is the Army's counsel assigned to this march-in. b5

b5

b5

I wanted to make sure you are aware of this request.

Kathy L. Hudson, Ph.D.
Deputy Director for Science, Outreach, and Policy
National Institutes of Health

301 496 1455
Kathy.hudson@nih.gov



National Institutes of Health
Turning Discovery into Health

REL0000024878



January 14, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: Sylvia.Burwell@hhs.gov

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892
Via: Francis.Collins@nih.hhs.gov

The Honorable Ashton Carter
Secretary
Department of Defense
1400 Defense Pentagon
Washington, D.C. 20301-1400
Via: ashton.b.carter.civ@mail.mil; whs.pentagon.esd.mbx.cmd-correspondence@mail.mil

Dear Secretaries Burwell and Carter and Director Collins:

Introduction

Knowledge Ecology International is a non-profit organization with offices in Washington, DC and Geneva, Switzerland. The Union for Affordable Cancer Treatment (UACT) is a non-profit cancer patient group. More about each group is available on their respective web pages: <http://keionline.org> and <http://cancerunion.org>.

This letter is a request that the U.S. federal government use its rights in patents for the prostate cancer drug (enzalutamide), marketed under the brand name of Xtandi by Japan-based Astellas

Pharma. This is a product that has an average wholesale price (AWP) of \$129,269 per year,¹ and which is far more expensive in the United States than in other countries.

Specifically, we ask the Department of Health and Human Services (DHHS), National Institutes of Health (NIH), and/or the Department of Defense (DoD) to use its royalty-free rights in the relevant patents, or to grant this request for march-in rights. The relevant patents include, but are not limited to, the three patents listed in the FDA Orange Book for Xtandi (7709517, 8183274, and 9126941), all of which were granted to the Regents of the University of California, a public institution. All three inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

The statutory basis for the request includes 35 U.S.C. § 202(c)(4), for the royalty-free rights in the patents, and 35 U.S.C. § 203(a)(1-3), noting that the term “practical application” of an invention in 35 U.S.C. § 203(a)(1) is defined by 35 U.S.C. § 201(f) to require that the benefits of an invention are “available to the public on reasonable terms.” It is our contention that the pricing of Xtandi is excessive and discriminatory as regards U.S. citizens.

Xtandi is an expensive drug everywhere, indeed so expensive that access is extremely limited in many countries. But, based upon our research, the prices in the United States are far higher than any other country in the world, despite the fact that the critical research benefited from U.S. taxpayer funded grants from the NIH and DoD.

More generally, we ask the U.S. federal government to adopt the policy that the federal government will use its royalty free rights, or grant licenses under federal march-in rights, when prices in the United States are excessive, and/or higher than they are in high income foreign countries, and to apply that policy in this case for patents on enzalutamide.

Such an approach would be in accord with the policy and objective of the Bayh-Dole Act as stated in 35 U.S.C. § 200, to “protect the public against nonuse **and** the unreasonable use of inventions...” [emphasis added].

The analysis in this document includes the following topics and tables.

1. Prices for Xtandi are much higher in the United States than in other high income countries,
2. The high prices for Xtandi create hardships on U.S. patients,
3. The cost of Xtandi to Medicare,
4. Astellas and Medivation projections of Xtandi sales,
5. The role of the U.S. government in funding research on Xtandi,
6. Enzalutamide is an important cancer drug,

¹ \$88.48 per 40 mg unit, four times a day, 365.25 days per year.

7. The University of California at Los Angeles (UCLA) interest in the patents,
8. Orange Book patent claims for Xtandi,
9. Non-patent exclusivity,
10. Generic supply,
11. Xtandi R&D investments through the 2012 approval for the lead indication,
12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA,
13. Licensing terms, including reasonable royalty,
14. Funding of research to further develop enzalutamide,
15. Standard for determining the Xtandi prices are unreasonable.
16. Conclusion

Tables:

Table 1.1: Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Table 2.1: Prior authorization requirements and formulary tiers for seven insurers providing reimbursements for Xtandi/enzalutamide

Table 3.1: Xtandi/Enzalutamide/Medicare Part D, 2012 to 2014

Table 4.1: Actual and projected Xtandi sales, FY2013 to FY2015

Table 4.2: Actual Xtandi sales, U.S., 2012 to 2014

Table 8.1: Xtandi Patents

Table 11.1: Trials Reported in FDA Medical Review for 2012 Approval for Xtandi

Table 11.2: Trial enrollment cited in in FDA medical reviews for lead indication of new drugs, 2010 to 2014

Table 11.3: R&D expenditures on Xtandi, 2005-2012 (in thousands of USD)

Table 11.4: R&D expenditures on Xtandi, 2013 and 2014 (in thousands of USD)

Table 12.1: Number of trials funded by Industry, NIH, other "U.S. Fed" and "Other," as reported in ClinicalTrials.Gov, January 6, 2016.

Table 12.2: Number of trials funded by Astellas and/or Medivation, as reported in ClinicalTrials.Gov, January 6, 2016.

Table 15.1: US Average Wholesale Price, relative to prices in reference countries

1. Prices for Xtandi are much higher in the United States than in other high income countries.

Xtandi is sold in 40 mg capsules or tablets, and is prescribed for daily use for as long as the drug continues to be effective and tolerated. The typical dose of Xtandi for the treatment of prostate cancer is 4 x 40 mg per day.

The U.S. average wholesale price (AWP), according to *Redbook* data published April 2015, was \$88.48 per 40 milligram capsule, which amounts to \$353.92 per day, or \$129,269.28 per year (365.25 day year). The average price for Medicare in 2014 was \$69.41 per capsule,² or \$101,408.01 for a full year's treatment.

Astellas Pharma, a Japanese-owned drug company, is exploiting the weak response of the United States to excessive pricing of drugs, and is charging U.S. consumers and third-party payers roughly two to four times as much as the prices in other high income countries. For example, in Norway, a country with a per capita income of \$103,630 in 2014, the price is \$32.43 per 40 mg capsule, just 47 percent of the US Medicare price, and 39 percent of the Redbook AWP for the U.S. private sector.

In Australia, the price is \$23.46 per capsule, roughly one third of the U.S. Medicare price. In Quebec, Canada, the price is \$20.12 per capsule, just 29 percent of the U.S. Medicare price, and 24 percent of the U.S. AWP.

Astellas Pharma, the company that holds the rights to market Xtandi, is a member of the Japan-based Mitsubishi UFJ Financial Group (MUFJ) keiretsu. Note that in Japan, the price per 40 mg unit of this UCLA-invented drug is \$26.37, less than one-third of the U.S. AWP.

In our opinion, it is unreasonable, and indeed outrageous, that prices are higher in the United States than in foreign countries, for a drug invented at UCLA using federal government grants.

² See Centers for Medicare and Medicaid Services Medicare Drug Spending Dashboard, available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Dashboard/Medicare-Drug-Spending/Drug_Spending_Dashboard.html

Table 1.1: Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Country	Price per unit, national currency		EX Rate (Jan. 6, 2016)	Price per unit, USD	Percent of 2015 AWP	2014, GNI Per Capita, Atlas Method, USD
USA, April 2015 AWP	88.48	USD	1	\$88.48	100%	\$55,200
USA, 2014 Medicare	69.41	USD	1	\$69.41	78%	\$55,200
Australia	33.04	AUD	0.71	\$23.46	27%	\$64,540
Belgium	29.15	EUR	1.08	\$31.48	36%	\$47,260
Canada, Quebec	28.35	CAN	0.71	\$20.12	23%	\$51,630
France	24.75	EUR	1.08	\$26.73	30%	\$42,960
Germany, public insurance	34.19	EUR	1.08	\$36.93	42%	\$47,640
Italy, procurement price	24.08	EUR	1.08	\$26.01	29%	\$34,270
Japan	3,138.80	Yen	0.0084	\$26.37	30%	\$42,000
The Netherlands	29.15	EUR	1.08	\$31.48	36%	\$51,890
Norway	294.78	NOK	0.11	\$32.43	37%	\$103,630
Spain	29.98	EUR	1.08	\$32.38	37%	\$29,440
Sweden	224.705	SEK	.12	\$26.96	30%	\$61,610
Switzerland	35.82	CHF	0.99	\$35.46	40%	\$88,120*
UK	24.42	GBP	1.46	\$35.65	40%	\$43,430

*Only 2013 was available for Switzerland.

2. The high prices for Xtandi create hardships on U.S. patients.

Recent clinical studies indicate that treatment delays may be harmful to patients. While the drug is relatively new, clinicians are now recommending that doctors prescribe Xtandi before prescribing other drugs that target the same androgen axis, to prevent the development of drug resistance.

Since 2014, the FDA has expanded the use of Xtandi to first line treatment for metastatic castration-resistant prostate cancer (mCRPC) based on the phase III PREVAIL clinical trial. Currently Xtandi (FDA approved, 2012), Zytiga (FDA approved, 2011), and Taxotere (FDA approved, 2004) are the top three prescribed drugs in first line metastatic CRPC treatment.³ However, using Taxotere before Xtandi has been shown to decrease the effectiveness of Xtandi

³ Flaig TW *et al.* Treatment evolution for metastatic castration-resistant prostate cancer with recent introduction of novel agents: retrospective analysis of real-world data. *Cancer Med.* 2015 Dec 29.

by a median overall survival of 15.8 months.⁴ Zytiga and Xtandi are both oral therapeutics that target the androgen signaling axis, and although prospective head-to-head comparison clinical trials are still ongoing, retrospective analysis data have indicated that there is a clear clinical cross-resistance between the two drugs.⁵ In fact, in a study conducted by Schrader *et al.*, it was reported that 48.6% of patients who previously took Zytiga and Taxotere were completely resistant to Xtandi.⁶ Based on the susceptibilities of individual patients, oncologists may want to prescribe Xtandi over Zytiga for its toxicity profile or to patients who cannot tolerate low-dose steroids.⁶ If insurance companies were to restrict the use of Xtandi in favor of Zytiga or Taxotere, it would likely prove detrimental to the survival of those patients.

As a direct result of the high price charged by Astellas, U.S. insurance companies and other third party payers have predictably restricted access to Xtandi. Insurers discourage prescribers by requiring restrictive prior authorizations that prevent use of Xtandi before a patient has failed other treatments. UnitedHealthcare, for example, noted in a memorandum that “Supply limits and/or Step Therapy may be in place.”⁷

Table 2.1 shows information from insurance formularies from across the United States, including whether prior authorization is required and what tier the insurer has placed the drug on in their formulary. Higher tiers generally indicate higher copays and restricted access, and insurers generally use 3- or 5-tier systems. (See the next section for a discussion of Medicare spending on Xtandi.)

Table 2.1: Prior authorization requirements and formulary tiers for seven insurers providing reimbursements for Xtandi/enzalutamide.

Payer	Formulary	Tier	Prior Authorization
Rocky Mountain Health Plans	Good Health Formulary ⁸	3	Yes
Kaiser Permanente	Exchange Formulary ⁹	4	No
Aetna	Three Tier Open Individual Formulary ¹⁰	3	Yes: step therapy
Cigna	Prescription Drug List ¹¹	5	Yes

⁴ Crawford ED *et al.* Treating Patients with Metastatic Castration Resistant Prostate Cancer: A Comprehensive Review of Available Therapies. J Urol. 2015 Dec;194(6):1537-47.

⁵ Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistant prostate cancer. Expert Opin Pharmacother. 2015 Mar;16(4):473-85.

⁶ Schrader AJ *et al.* Enzalutamide in castration-resistant prostate cancer patients progressing after docetaxel and abiraterone. Eur Urol. 2014 Jan;65(1):30-6.

⁷ <https://goo.gl/PFtBkf>

⁸ http://www.rmhp.org/docs/default-source/resources/good_health_formulary.pdf?sfvrsn=10

⁹ https://healthy.kaiserpermanente.org/static/health/pdfs/formulary/mid/mid_exchange_formulary.pdf

¹⁰ <https://goo.gl/Z31uvf>

¹¹ <http://www.cigna.com/individuals-families/prescription-drug-list?consumerID=cigna&indicator=IFP>

BlueCross BlueShield	Federal Employee Program ¹²	4	Yes
Montana Health CO-OP	2015 CoventryOne Prescription Drug List ¹³	4	Yes
Anthem BlueCross	Select Drug List 4-Tier Formulary ¹⁴	4	Yes

There is also a racial disparity in the incidence, mortality, and treatment of prostate cancer. NIH and DoD should be concerned that the high price of Xtandi may be contributing to systemic racial discrimination in medical care in the United States. Data collected by the Centers for Disease Control shows that African American men have higher incidence and mortality rates than all other populations. Around two times more African American men have prostate cancer than white men (graph 2.1), and around 2.5 times more African American men die from the disease compared to white men (graph 2.2).¹⁵ In addition, African American men are more likely to have a more aggressive form of prostate cancer. Researchers believe that this racial disparity is the result of sociobiological factors that affect people of African descent.

Beyond sociobiological effects on incidence, mortality, and severity of prostate cancer, African American men face systemic discrimination that affects their access to and quality of treatment. One recent study has found that African-American men on Medicare being treated for nonmetastatic prostate cancer experienced treatment delays, and had more postoperative emergency room visits and readmissions compared to white men.¹⁶ “This might be a form of institutional discrimination based on socioeconomic status resulting in racially disparate outcomes,” wrote Dr. Otis Brawley, chief medical officer of the American Cancer Society, commenting on that study.¹⁷

¹² https://media.fepblue.org/-/media/PDFs/Brochures/FEP_AbbreviatedFormulary_100715.pdf

¹³ <http://www.mhc.coop/wp-content/uploads/docs/MHC-Covered-Drugs.pdf>

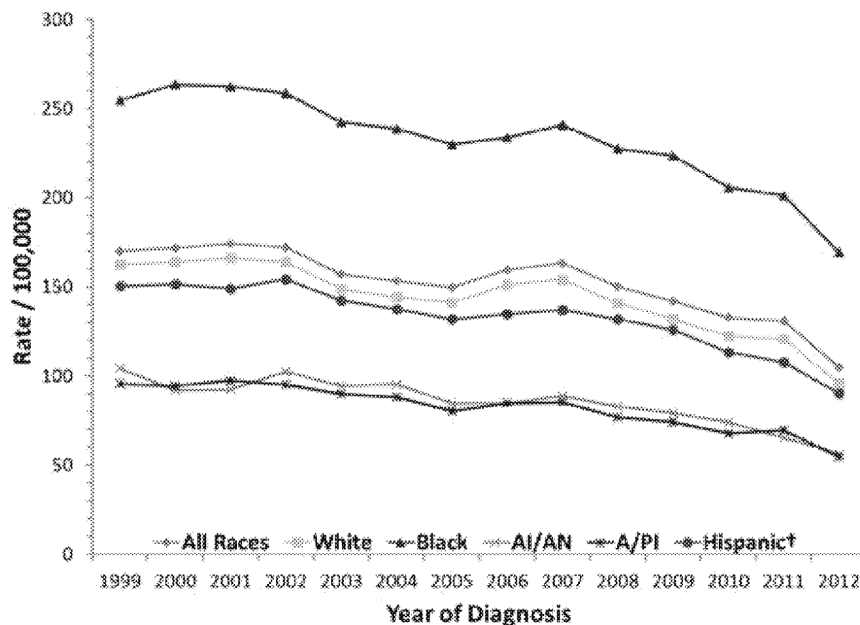
¹⁴ https://fm.formularynavigator.com/MemberPages/pdf/2016CAsSelectHIX_7006_Full_1576.pdf

¹⁵ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>.

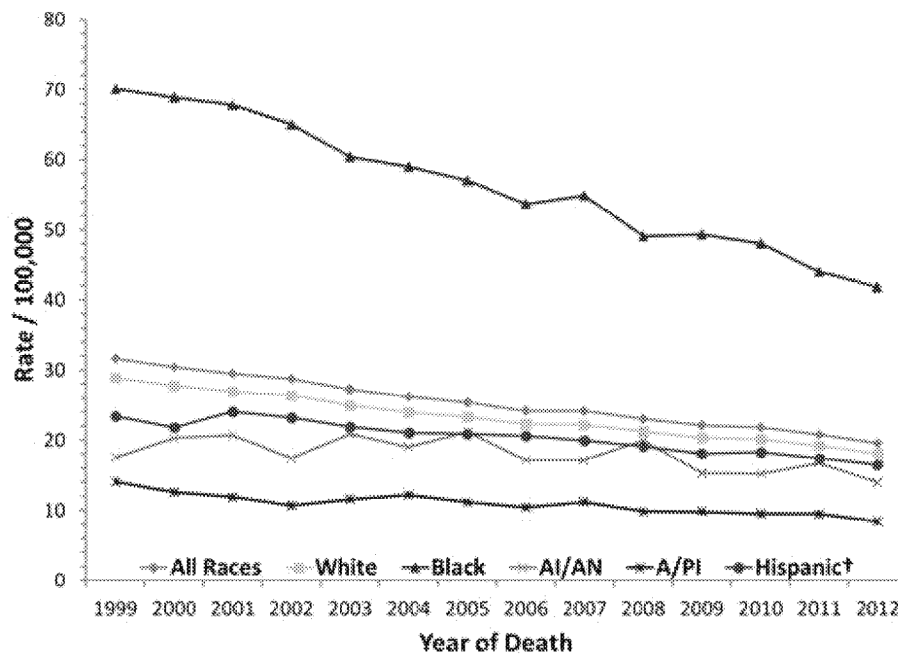
¹⁶ Schmid M et al. Racial differences in the surgical care of Medicare beneficiaries with localized prostate cancer. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3384

¹⁷ Brawley OW. The meaning of race in prostate cancer treatment. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3615

Graph 2.1: “Prostate Cancer Incidence Rates by Race and Ethnicity, U.S., 1999–2012”¹⁸



Graph 2.2: “Prostate Cancer Death Rates by Race and Ethnicity, U.S., 1999–2012”¹⁹



¹⁸ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>, which contains additional notes on the data/methodologies used to create graphs 1 and 2 in this letter.

¹⁹ See CDC, “Prostate Cancer Rates by Race and Ethnicity,” available at <http://www.cdc.gov/cancer/prostate/statistics/race.htm>.

Veterans who served in Vietnam and the Korean demilitarized zone, who may have been exposed to Agent Orange, are also at higher risk for more aggressive forms of prostate cancer, according to a study conducted by the Department of Veterans Affairs and Oregon Health and Science University.²⁰

3. The cost of Xtandi to Medicare.

According to the Centers for Medicare and Medicaid Services, total Medicare spending on Xtandi grew dramatically from under \$35 million in 2012 to nearly \$447 million in 2014. The increase in outlays from 2013 to 2014 was 93 percent. Part of that growth was due to a 9 percent price increase from 2012 to 2014, a period in which the Consumer Price Index (CPI) grew a mere 3 percent. There was also a steep increase in the number of patients, from 2,143 in 2012, to 7,329 in 2013, and 11,800 in 2014.

Table 3.1: Xtandi/Enzalutamide/Medicare Part D, 2012 to 2014

Year	Total Spending	Beneficiary Cost Share	Beneficiary Count	Total Annual Spending Per User	Avg Cost Per Unit	Claim Count
2012	\$34,898,755.93	\$2,359,870.77	2,143	\$16,285.00	\$63.72	4,519
2013	\$231,503,731.19	\$13,276,790.11	7,329	\$31,587.36	\$64.85	29,572
2014	\$447,311,084.46	\$24,567,059.52	11,800	\$37,907.72	\$69.41	53,980

For prostate cancer, the average age at diagnosis is 66 years. At present, approximately 14 percent of the population is 65 or over, but in five years this will increase to 16 percent, and by 2030 is expected to exceed 19 percent. As the population continues to age, we can reasonably predict that Medicare expenditures on Xtandi will continue to climb.

4. Astellas and Medivation projections of Xtandi sales.

According to the Astellas 2015 annual report,²¹ the United States market will represent 61.16 percent of all global sales of Xtandi, for the fiscal year ending March 31, 2016. Note that in the U.S., sales of Xtandi increased 77 percent from FY2013 (April 1, 2013 to March 31, 2014) to FY2014 (April 1, 2014 to March 31, 2015), and are projected to increase 51 percent from FY2014 to FY2015. This is a steep increase in use for a costly drug.

²⁰ Ansbaugh N et al. Agent Orange as a risk factor for high-grade prostate cancer. Cancer. 2013 Jul; 119(13):2399-2404. Available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4090241/>.

²¹ Astellas Annual Report 2015, available at https://www.astellas.com/en/ir/library/pdf/2015AR_en_1007-2.pdf.

Table 4.1: Actual and projected Xtandi sales, FY2013 to FY2015²²

Country/Region	FY2013	FY2014	FY2015 (projected)
Japan		\$125,147,037	\$193,179,990
U.S.	\$441,000,000	\$779,000,000	\$1,180,000,000
Percent Change in Sales, U.S.		77%	51%
Other Americas	\$8,000,000	\$24,000,000	\$35,000,000
Europe, Middle East, and Africa	\$75,255,950	\$259,095,485	\$505,289,950
Asia/Oceania		\$5,039,478	\$15,958,347
Global	\$524,255,950	\$1,192,282,001	\$1,929,428,288
Percent U.S. Sales to Global	84%	65%	61%

Astellas developed Xtandi in collaboration with Medivation. The Medivation 2015 SEC 10-K filing reports actual Xtandi sales in the United States for calendar years 2012 to 2014.

Medicare's share of sales have increased sharply since 2012. In 2014 they accounted for 66 percent of Xtandi's overall U.S. sales, and 42 percent of global sales. The United States is the largest spender on Xtandi, and most of that money is coming from taxpayers and the insurance payments of aging Americans.

Table 4.2: Actual Xtandi sales, U.S., 2012 to 2014²³

Calendar Year	2012	2013	2014
Xtandi U.S. Sales	\$71,504,000	\$392,415,000	\$679,805,000
Percent Change in U.S. Sales		449% ²⁴	73%
Xtandi Non-U.S. Sales		\$52,800,000 ²⁵	\$381,100,000
Medicare Total Spending	\$34,898,755.93	\$231,503,731.19	\$447,311,084.46
Medicare Share of U.S. Sales	49%	59%	66%
Medicare Share of Global Sales	49%	52%	42%

²² Astellas defines its fiscal year as April 1 to March 31, beginning in the year indicated. Monetary amounts were converted to USD from regional currencies, as necessary.

²³ Medivation 2015 Form 10-K, available at

<http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf>.

²⁴ Note: Xtandi was approved on August 12, 2012, which accounts for low sales.

²⁵ Note: Xtandi was first approved outside the U.S. in June 2013, which accounts for low sales.

5. The role of the U.S. government in funding research on Xtandi.

As noted above, all three patents in the Orange Book for Xtandi disclose the fact that the inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

In addition to the grants listed in these three patents, the development of this drug benefited from additional research subsidies from the federal government and charitable foundations, including grants for clinical testing of the drug. For example, a 2009 paper in *Science* reporting on the development of MDV3100 (the development name for enzalutamide)²⁶ acknowledged funding from the Prostate Cancer Foundation, the National Cancer Institute, the DOD PC051382 Prostate Cancer Research Program Clinical Consortium Award, and support from the Charles H. Revson Foundation. Likewise, a 2010 paper in *the Lancet* reporting on a critical Phase 1-2 trial acknowledges the financial support of Medivation, but also the Prostate Cancer Foundation, National Cancer Institute, the Howard Hughes Medical Institute, Doris Duke Charitable Foundation, and Department of Defense Prostate Cancer Clinical Trials Consortium.

27

6. Enzalutamide is an important cancer drug.

In the United States today there are nearly 3 million men suffering from prostate cancer, with over 220,000 new cases in 2015 alone, and 27,540 deaths. It is the third most common form of cancer in the U.S.

When patients are treated early and tumors are localized, the prognosis is often favorable. However, some patients will relapse, leading in nearly all cases to castration resistant prostate cancer (CRPC). At the CRPC stage, the disease is no longer responsive to androgen deprivation therapy (ADT), thus limiting the available treatment options with a greater disease burden. Access to Xtandi/enzalutamide, a non-steroidal second generation androgen receptor agonist, becomes critical to extending the life of the patient, and allowing patients to live an improved quality of life.

There are currently six treatments being used to treat CRPC. Xtandi/enzalutamide has several advantages over the other treatments. Four of the treatments are invasive and require I.V. administration, leukapheresis, or the use of radiopharmaceuticals. Xtandi/enzalutamide and Zytiga are the only daily oral tablets. However Xtandi/enzalutamide's pill burden is lighter since

²⁶ Tran C *et al.* Development of a second-generation antiandrogen for treatment of advanced prostate cancer. *Science*. 2009. May. 8;324(5928):787-90.

²⁷ Scher HI *et al.* Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study, *Lancet*. 2010 Apr 24;375(9724):1437-46. doi: 10.1016/S0140-6736(10)60172-9.

it does not need to be taken in combination with prednisone. As such, Xtandi/enzalutamide is well tolerated and has more favorable toxicity profile.

Quality of life was also more frequently improved and median time to deterioration was significantly longer with Xtandi/enzalutamide compared to placebo, as reported by patients in functional assessment questionnaires administered during clinical trials.²⁸

With recent and ongoing clinical trials reporting better prostate cancer control when Xtandi/enzalutamide is used in chemotherapy naive CRPC cases or in combination with other agents, it is expected that this drug will soon be prescribed to wider subset of patients.^{29,30,31} In fact experts say that in the next 3 years all CRPC will progress to Xtandi or Zytiga.³²

Xtandi/enzalutamide is also being tested for other types of cancer, including clinical trials for breast cancer (triple negative³³, her2+³⁴), hepatocellular carcinoma³⁵, bladder cancer³⁶, ovarian or fallopian tube cancer,³⁷ pancreatic cancer³⁸ and Mantle Cell Lymphoma³⁹.

7. The University of California at Los Angeles (UCLA) interest in the patents

According to the Medivation's 2014 10-K report to the Securities and Exchange Commission (SEC), the University of California at Los Angeles (UCLA) licensed the patents for the drug to Medivation in exchange for an annual payment of \$2.8 million, a 4 percent royalty on global net sales of the drug, and in addition a 10 percent share of Medivation's sublicensing income

²⁸ Rodriguez-Vida A *et al.* Enzalutamide for the treatment of metastatic castration-resistant prostate cancer. *Drug Des Devel Ther.* 2015 Jun 29;9

²⁹ Scher HI *et al.* Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med.* 2012 Sep.

³⁰ Lortot Y *et al.* Effect of enzalutamide on health-related quality of life, pain, and skeletal-related events in asymptomatic and minimally symptomatic, chemotherapy-naïve patients with metastatic castration-resistant prostate cancer (PREVAIL): results from a randomised, phase 3 trial. *Lancet Oncol.* 2015 May.

³¹ STRIDE results presented at 2015 American Society of Clinical Oncology annual meeting, [Clinicaltrials.gov:NCT01981122](http://Clinicaltrials.gov/NCT01981122).

³² Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistant prostate cancer. *Expert Opin Pharmacother.* 2015 Mar;16(4):473-85.

³³ NCT01889238.

³⁴ NCT02091960.

³⁵ NCT02528643, NCT02642913. Hepatocellular carcinoma (HCC, also called malignant hepatoma) is the most common type of liver cancer, often secondary to a viral hepatitis infection (hepatitis B or C) or cirrhosis.

³⁶ NCT02605863, NCT02300610.

³⁷ NCT02300610.

³⁸ NCT02138383.

³⁹ NCT02489123. Mantle cell lymphoma (MCL) is a rare, B-cell NHL that most often affects men over the age of 60.

derived from the Astellas Collaboration Agreement.⁴⁰ The Astellas Collaboration Agreement has separate terms for U.S. and non-U.S. sales, as described below:

Medivation 2014 10-K

p.121:

(c) License Agreement with UCLA

Under an August 2005 license agreement with UCLA, the Company's subsidiary Medivation Prostate Therapeutics, Inc. holds an exclusive worldwide license under several UCLA patents and patent applications covering XTANDI and related compounds. Under the Astellas Collaboration Agreement, the Company granted Astellas a sublicense under the patent rights licensed to it by UCLA.

The Company is required to pay UCLA (a) an annual maintenance fee, (b) \$2.8 million in aggregate milestone payments upon achievement of certain development and regulatory milestone events with respect to XTANDI (all of which has been paid as of December 31, 2014), (c) ten percent of all Sublicensing Income, as defined in the agreement, which the Company earns under the Astellas Collaboration Agreement, and (d) a four percent royalty on global net sales of XTANDI, as defined.

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p.104-105

(c) Collaboration Revenue

Collaboration revenue consists of three components: (a) collaboration revenue related to U.S. XTANDI sales; (b) collaboration revenue related to ex-U.S. XTANDI sales; and (c) collaboration revenue related to upfront and milestone payments.

[...]

Collaboration Revenue Related to U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all U.S. XTANDI sales. The Company and Astellas share equally all pre-tax profits and losses from U.S. XTANDI sales. Subject to certain exceptions, the Company and Astellas also share equally all XTANDI development and commercialization costs attributable to the U.S. market, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA. The primary exceptions to the equal cost sharing are that each party is responsible for its own commercial FTE costs and that development costs supporting marketing approvals in both the United States and either Europe or Japan are borne one-third by the Company and two-thirds by Astellas. The Company recognizes collaboration revenue related to U.S. XTANDI sales in the period in

⁴⁰ UNITED STATES SECURITIES AND EXCHANGE COMMISSION, Form 10-K, For the Fiscal Year Ended December 31, 2014, <http://www.sec.gov/Archives/edgar/data/1011835/000119312515062576/d850483d10k.htm>

which such sales occur. Collaboration revenue related to U.S. XTANDI sales consists of the Company's share of pre-tax profits and losses from U.S. sales, plus reimbursement of the Company's share of reimbursable U.S. development and commercialization costs. The Company's collaboration revenue related to U.S. XTANDI sales in any given period is equal to 50% of U.S. XTANDI net sales as reported by Astellas for the applicable period.

[...]

Collaboration Revenue Related to Ex-U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all ex-U.S. XTANDI sales. Astellas is responsible for all development and commercialization costs for XTANDI outside the United States, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA, and pays the Company a tiered royalty ranging from the low teens to the low twenties on net ex-U.S. XTANDI sales. The Company recognizes collaboration revenue related to ex-U.S. XTANDI sales in the period in which such sales occur. Collaboration revenue related to ex-U.S. XTANDI sales consists of royalties from Astellas on those sales.

[...]

Medivation came to acquire rights to Xtandi from UCLA through an agreement initiated by Dr. Charles L. Sawyers and Dr. Michael E. Jung, researchers at UCLA working on prostate cancer screening techniques and treatments. Dr. Sawyers is an oncologist who currently runs a lab at Memorial Sloan Kettering Cancer Center and serves on the Board of Directors for Novartis.⁴¹ He was a key participant in the development of Gleevec and Sprycel, and is a recipient of the Lasker Award. Dr. Michael E. Jung is a Distinguished Professor of Chemistry at UCLA, where he runs a lab that conducts research on chemicals related to the treatment of cancer.

Dr. Sawyers approached Medivation through its founder, Dr. David Hung, a former colleague at the University of California, San Francisco. They settled on an agreement that required Dr. Sawyers and Dr. Jung to disclose all molecules related to their prostate cancer research that benefitted from Medivation funding. Dr. Sawyers served on Medivation's Scientific Advisory Board, as did Dr. Jung, receiving \$20,000 and \$400,000 worth of stocks, respectively.

In addition, Dr. Sawyers and Dr. Jung used the fruits of their research to found their own pharmaceutical firm, Aragon Pharmaceuticals, which they used as a vehicle to develop a drug with a very similar chemical structure to Xtandi. Medivation sued the doctors, Aragon, and UCLA, over the development of that drug.⁴² According to SEC filings, Medivation and UCLA are now engaged in separate litigation over licensing payments on Xtandi.⁴³

⁴¹ More on Dr. Sawyers is available here:

<http://www.bloomberg.com/research/stocks/private/person.asp?personId=12631592&privcapId=25460204>.

⁴² For an amended complaint, filed February 9, 2012, see here: <https://goo.gl/p3lpnm>.

⁴³ Medivation 2015 10-K SEC filing, available here:

<http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf>.

8. Orange Book patent claims for Xtandi

As noted above, Astellas has listed three patents in the FDA Orange book for Xtandi sales. These include US patent number 7709517, for both a drug substance and drug product claim, and two additional patents, US patent numbers 8183274 and 9126941.

Table 8.1: Xtandi Patents

Patent Number	7,709,517	8,183,274	9,126,941
Title:	Diarylhydantoin compounds	Treatment of hyperproliferative disorders with diarylhydantoin	Treatment of hyperproliferative disorders with diarylhydantoin compounds
Publication date	May 4, 2010	May 22, 2012	Sep 8, 2015
Filing date	May 15, 2006	Feb 18, 2010	Apr 17, 2012
Priority Date	May 13, 2005	May 13, 2005	May 13, 2005
Inventors	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Derek Welsbie, Chris Tran, John Wongvipat, Dongwon Yoo	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat
Original Assignee	The Regents Of The University Of California	The Regents Of The University Of California	The Regents Of The University Of California
Expiration date	Aug 13, 2027	May 15, 2026	May 15, 2026
FDA substance claim	Yes		
FDA product claim	Yes		
FDA use claim code		U - 1281; The treatment of patients with metastatic castration-resistant prostate cancer (CRPC) who have previously	U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

		received docetaxel. U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).	
Disclosure of US rights in the patent	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with Government support under Grant No. W81XWH-04-1-0129 awarded by the United States Army, Medical Research and Materiel Command; Grant No. CA092131 awarded by the National Institutes of Health. The Government has certain rights in this invention.

9. Non-patent exclusivity.

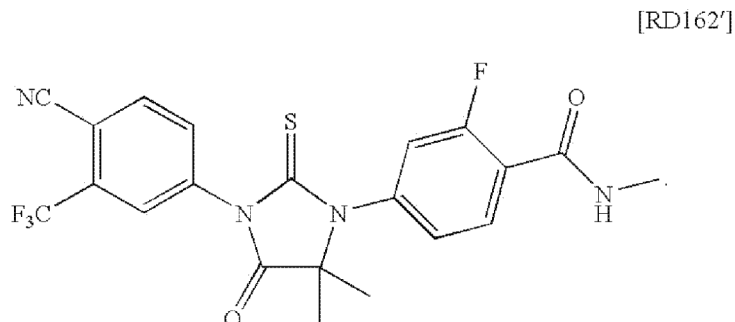
The FDA Orange Book lists two grants of non-patent exclusivity to Astellas for enzalutamide, both expiring in 2017. One was granted for enzalutamide as a new chemical entity, expiring August 31, 2017; the second was granted under code I-693 for “treatment of patients with metastatic castration-resistant prostate cancer (CRPC)”, expiring September 10, 2017. These dates are sufficiently close that they should not be used to excuse non-action on this request, particularly since it may take several months for a generic supplier to prepare data for an Abbreviated New Drug Application (ANDA).

10. Generic supply

Enzalutamide is a small molecule drug that does not have a complex structure.

Enzalutamide is a synthetic, non-steroidal pure antiandrogen, originally named MDV3100, which has the formula $C_{21}H_{16}F_4N_4O_2S$, a molar mass of 464.44 g/mol and a chemical name of 4-(3-(4-Cyano-3-(trifluoromethyl)phenyl)-5,5-dimethyl-4-oxo-2-thioxoimidazolidin-1-yl)-2-fluoro-N-methylbenzamide. The chemical structure, illustrated in Figure 1, includes a thiohydantoin and two benzene groups.

Figure 10.1: Structure of MDV3100 (CAS number: 915087-33-1)



Petitioners have excellent relations with several generic drug manufacturers, and do not anticipate difficulties obtaining the necessary FDA approvals for generic versions of enzalutamide, once the federal government provides access to the patents, either by using the royalty-free right in the patents or granting this march-in request.

Note that the 2015 U.S. AWP for Xtandi of \$88.48 per 40 mg capsule is equivalent to \$2,212 per gram of active pharmaceutical ingredient.

Generic products with similar complexity for manufacturing can be obtained for under \$10 per gram of API, retail,⁴⁴ and considerably less in bulk.

11. Xtandi R&D investments through the 2012 approval for the lead indication

Xtandi was approved as a treatment for prostate cancer in August 31, 2012, as a priority drug under the FDA Priority Review program. The application was by Astellas, and was approved by the FDA as NDA 203415.

The application for the NDA was supported by evidence from four clinical trials, including one Phase 1 trial with 140 patients enrolled, one Phase 1/2 trial with 27 patients enrolled, one Phase 2 trial with 60 patients enrolled, and one Phase 3 trial with 1,199 patients enrolled. Total enrollment for the 4 trials was 1,426 patients.

⁴⁴ For example, generic versions of the cancer drug imatinib.

Table 11.1: Trials Reported in FDA Medical Review for 2012 Approval for Xtandi

Study Number	NCT Number	Phase	Start- End Date	Enrolled (FDA Review)	Study Sponsor	Federal Funding
S-3100-1-01	NCT00510718	1	7/2007- 1/2010	140	Medivation	NCI, DoD ⁴⁵
CRPC-MDA-1	NCT01091103	2	2/2010- 7/2011	60	Medivation	NCI, DoD ⁴⁶
CRPC2	NCT00974311	3	9/2009- 9/2011	1199	Medivation	n/a
9785-CL-0111	NCT01284920	1/2	11/2010- 7/2012	27	Astellas Pharma	n/a

The two earliest trials (NCT00510718, NCT01091103) received subsidies from the National Cancer Institute and Department of Defense, in addition to funding from the Prostate Cancer Foundation and other non-profit institutions. After receiving favorable results from the trials subsidized by NCI and DoD, Medivation and Astellas funded two additional trials.

The size of the trials for Xtandi were typical of other cancer drugs approved from 2010 to 2014 for the lead indication as a New Molecular Entity, and much smaller than trials used to approve non-cancer drugs.

Table 11.2: Trial enrollment cited in in FDA medical reviews for lead indication of new drugs, 2010 to 2014

Average for all cancer drugs	1,316
Average for non-Cancer Drugs	4,733
Xtandi	1,426

Medivation reported their direct expenditures and cost-sharing payments from Astellas for collaboration on the development of Xtandi between 2005 and 2012, when the FDA granted Xtandi marketing approval. They defined direct costs as “clinical and preclinical study costs, cost of supplying drug substance and drug product for use in clinical and preclinical studies, contract research organization fees, and other contracted services pertaining to specific clinical and preclinical studies.”⁴⁷ The number reported excludes indirect costs, which include “administrative and support costs.”⁴⁸

Astellas contributed to half of all direct costs for R&D conducted for U.S. drug approval, two-thirds of costs for R&D directed towards trials aimed at both U.S. and non-U.S. use of

⁴⁵ Scher, Howard I., et al. "Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1–2 study." *The Lancet* 375.9724 (2010): 1437-1446.

⁴⁶ Efsthathiou, Eleni, et al. "Molecular characterization of enzalutamide-treated bone metastatic castration-resistant prostate cancer." *European urology* 67.1 (2015): 53-60.

⁴⁷ Medivation 2009 10-K SEC filing, available here:

<http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-10-57020/1011835/filing.pdf>.

⁴⁸ Ibid. Indirect costs for all drugs combined are available in Medivation SEC filings.

Xtandi, and full development costs for commercialization outside the United States. Based upon the Medivation SEC filings, R&D outlays on Xtandi were \$303 million through the end of the calendar year 2012.

Table 11.3: R&D expenditures on Xtandi, 2005-2012 (in thousands of USD)

SEC 10-K Year	2005	2006	2007	2008	2009	2010	2011	2012
Medivation Direct Costs	\$261	\$3,021	\$2,619	\$8,845	\$27,046	\$23,454	\$42,3350	\$67,086
Development cost-sharing payments from Astellas					\$2,784	\$34,125	\$44,285	\$47,473
Total	\$261	\$3,021	\$2,619	\$8,845	\$29,830	\$57,579	\$86,620	\$114,559
Cumulative Total								\$303,334

Medivation reported outlays of an additional \$285 million in calendar years 2013 and 2014, much of that money aimed at justifying broader use of Xtandi for prostate cancer, but also on testing the drug to treat other types of cancer.

Table 11.4: R&D expenditures on Xtandi, 2013 and 2014 (in thousands of USD)

SEC 10-K Year	2013	2014
Medivation Direct Costs	\$73,076	\$102,669
Development cost-sharing payments from Astella	\$46,594	\$63,479
Total	\$119,670	\$166,148
Cumulative Total		\$285,818

The company outlays on R&D investments were significant, although it is worth noting that the early and most risky trials were small and subsidized by the United States government.

Note that through the end of 2014, representing a little more than two years of reimbursements, Medicare spent \$704 million on Xtandi. Astellas expects a sharp increase in U.S. sales in 2015 and 2016, and the company revenues also include sales from non-Medicare patients in the United States and patients outside of the United States.

12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA.

Like many cancer drugs, the initial approval of the drug for the lead indication has lead to continued research to determine the best uses of the drugs, both for prostate cancer patients and to test the benefits of using enzalutamide to treat other types of cancer.

As of January 6, 2015, there were 129 trials listed in the ClinicalTrials.Gov database.

The funding of the trials is reported under the categories Industry, U.S. Fed., NIH, and Other, as well as combinations of those categories.

- 54 of the 129 trials were reported as funded by Industry alone.
- Another 31 trials were reported as funded by Industry and some other funder.
- The NIH or other U.S. Federal agencies were reported as funders in whole or in part of 18 trials.
- The category “Other” is quite important, accounting for 29 trials funded exclusively by Other, and another 42 where “Other” is among the funders.

Many of the trials funded by “Other” refer to universities and other non-profit research organizations that receive NIH or other federal agency research grants. “Other” also refers to funding from foreign governments and charities.

Table 12.1: Number of trials funded by Industry, NIH, other “U.S. Fed” and “Other,” as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
“Industry” only	54
Mixed including “Industry”	31
“Other” only	29
Mixed including “Other”	42
NIH only	3
Mixed including NIH or other “U.S. Fed”	16

Table 12.2: Number of trials funded by Astellas and/or Medivation, as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
Astellas and/or Medivation as sponsor of industry only funded trials	39
Astellas and/or Medivation as sponsor of mixed funded trials	18

Among the trials funded in whole or in part by “Industry”, the majority, 57, were funded by Astellas and/or Medivation, and of those only for 39 (30 percent of the 129) were they the sole funder of the trials.

Other companies, such as Lilly, Gilead, Roche, Bayer, Sanofi, and smaller companies, were involved in funding 28 trials.

13. Licensing terms, including reasonable royalty.

We are requesting the federal government grant an open license to any generic drug manufacturer.

The federal government has no obligation to pay royalties on the patents when and if it exercises its royalty free rights in the patents.

If the government orders the licensing of the patents under the federal march-in statutes, the terms of the license, including the royalty, have to be “reasonable under the circumstances.”⁴⁹

The issue of the appropriate royalty rate can be briefed and argued when and if the federal government is inclined to exercise march-in rights on the patent.

“Under the circumstances” would include many factors, such as that the facts motivating the granting of the march-in request are related to abuses of the patent rights, including in particular charging an excessive price and discriminating against U.S. consumers.

Rights in test data

Patents are granted for inventions, but as noted above, patents are not the only intellectual property rights associated with drug development.

The FDA provides additional intellectual property rights for investments in clinical trials, including five years of exclusive rights to rely upon data supporting the registration of a new chemical entity, and three years of rights in the data to support new indications on a drug.

The five years of test data exclusivity for Xtandi as a treatment for patients with metastatic castration-resistant prostate cancer (CRPC) will expire on September 10, 2017 in the United States, and later in many other countries. For example, the term of protection for test data is up to 8 years in Japan and Canada, and 11 years in the European Union.⁵⁰ The rights in test data are designed to protect and reward investments in clinical trials, and they operate separately from patent protection. The existence of the test data rights eliminates the need to consider investments in clinical trials when considering the royalty to the patent holder, because those investments are protected by this separate intellectual property right. As regards the

⁴⁹ 35 USC 203(a).

⁵⁰ Comparison of the Non-patent Drug Exclusivities Available in the United States, Canada, Europe and Japan. The International Economic Forum of the Americas. Serge Lapointe, Ph.D. June 14, 2012 <http://forum-americas.org/sites/default/files/documents/20120614-lapointe-pres.pdf>

investments in the U.S. market, it is likely that Astellas will have earned more than \$5 billion from the U.S. market alone, through September 10, 2017, the date of the most relevant test data exclusivity in the United States ends. Astellas will have also earned billions more from sales outside of the United States, where most patients reside.

Average industry royalty rates

According to the IRS, in 2012, the average rate of aggregate royalties (for all patents, know-how, trademarks, etc.⁵¹), reported on corporate income tax returns for the pharmaceutical and medicine manufacturing sector (MINOR CODE 325410) was 6.95 percent.

14. Funding of research to further develop enzalutamide.

One possible argument against any policy that lowers drug prices or shortens the term of a monopoly is that society benefits from the incentive to invest in R&D to find new uses for a drug.

It is possible to address the objective of providing sustainable sources of R&D funding without having high prices or longer monopolies.

On at least two occasions in the past involving NIH funded cancer drugs, and more recently in connection with proposals to create or extend monopolies in various drafts of the 21st Century Cures Act, there have been proposals to have mandates for funding R&D.

In one case, involving a dispute over the term of the monopoly on the cancer drug cisplatin in the early 1980s, there was a proposal that generic firms be obligated to contribute to the costs of ongoing research to determine new uses for the drug, following generic entry. This proposal, made by a generic drug company seeking to end the cisplatin monopoly, led to a compromise whereby Bristol-Myers was allowed to extend the monopoly for five more years, but only after they lowered the price of cisplatin and contributed tens of millions of dollars to independent research through non-profit institutions, at the direction of the NIH. Later, BMS proposed something similar, in an unsuccessful effort to extend data exclusivity on the cancer drug Taxol. In early drafts of the the 21st Century Cures legislation, there were proposals to associate extensions of drug monopolies with obligations to provide money to the NIH, and to make other investments in R&D.

In this case involving Xtandi, the NIH could simultaneously end the Xtandi monopoly and require any generic drug company to make contributions toward follow-on research to explore new and/or better uses of enzalutamide. Such obligations could be a condition of any use of the federal government's royalty free right in the drug, or as a condition of obtaining a march-in license.

⁵¹ The IRS does not provide a definition of royalties. See: <https://www.irs.gov/pub/irs-tege/eotopicd89.pdf>.

Note that there are benefits in having different parties participate in the testing of drugs, including those that do not have conflicts of interest as regards reporting possible negative impact of products, or allowing greater competition in designing better delivery mechanisms or new combination products. Also, in the case of Xtandi, more than half of the trials involving enzalutamide are already funded by entities other than Astellas.

15. Standard for determining that Xtandi prices are unreasonable.

In determining if the prices for Xtandi violate the statutory obligation to make products available to the public on reasonable terms and conditions, the NIH has broad discretion to consider a variety of factors, including the high price of the drug and the fact that the high price leads to restrictions on access and financial hardships on patients. However, in this case, we recommend the NIH address a narrower question, that can be answered clearly, given the robust evidence.

Do the Astellas prices for Xtandi discriminate against consumers in the United States? And, if so, the NIH should approve the March-In request, or use its royalty free rights in the patents, to prevent U.S. residents from paying more for a drug invented on federal grants than residents of other high income countries.

We have obtained prices for Xtandi in the United States and in 13 other high income countries, and this data allows the NIH to determine whether U.S. consumers are being asked to pay more for a drug invented on federal grants than Astellas charges in other high income countries.

One possible comparison to determine if the price is unreasonable is to consider the prices in other industrialized countries outside of the United States that have (1) per capita incomes of at least half that of the United States, (2) have the large economies as measured by the GDP, and (3) are members of the OECD, and to consider the U.S. price to be unreasonable, if the average wholesale price (AWP) in the U.S. is higher than the median price in the reference countries.

We propose using an odd number of countries. The 13 countries that have incomes at least 50 percent of the United States and which have the largest economies include Japan, Germany, France, the UK, Italy, Canada, Australia, Spain, the Netherlands, Switzerland, Sweden, Belgium and Norway.

We have prices for all 13 of the reference countries. None of the prices are higher than \$36.93, and the April 2015 U.S. AWP was \$88.48. It is not a close call: the U.S. prices are discriminatory and are unfair to U.S. residents. Note that the *highest* price of the 13 high income reference countries was less than half (42 percent) of the average wholesale price (AWP) in the United States, the median of the 13 prices reference prices we have obtained is just 36 percent of the US AWP, and the prices in Japan and Canada are 30 percent and 23 percent respectively of US AWP. As a percentage in 2014 per capita income, the U.S. prices are also

far higher than for any of the 13 high income countries. In eight countries, the annual cost of Xtandi is between 47 percent and 97 percent of annual per capita income. In four countries, the annual cost of Xtandi is between 111 percent and 161 percent of per capita income. In the United States, the annual cost of Xtandi is 234 percent of 2014 per capita income.

Table 15.1: US Average Wholesale Price, relative to prices in 13 reference countries

	2014 GDP	2014 annual Per Capita Income	price per 40 mg unit	Annual price (x 4x 365.25) as percent of 2014 per capita income
United States, Average Wholesale price April 2015	\$17,419,000,000,000	\$55,200	\$88.48	234%
Japan	\$4,601,461,206,885	\$42,000	\$26.37	92%
Germany	\$3,868,291,231,824	\$47,640	\$36.93	113%
France	\$2,829,192,039,172	\$42,960	\$26.73	91%
United Kingdom	\$2,988,893,283,565	\$43,430	\$35.65	120%
Italy	\$2,141,161,325,367	\$34,270	\$26.01	111%
Canada	\$1,785,386,649,602	\$51,630	\$20.12	57%
Australia	\$1,454,675,479,666	\$64,540	\$23.46	53%
Spain	\$1,381,342,101,736	\$29,440	\$32.38	161%
Netherlands	\$879,319,321,495	\$51,890	\$31.48	89%
Switzerland	\$701,037,135,966	\$88,120*	\$35.46	59%
Sweden	\$571,090,480,171	\$61,610	\$26.96	64%
Belgium	\$531,546,586,179	\$47,260	\$31.48	97%
Norway	\$499,817,138,323	\$103,630	\$33.09	47%
Median, reference countries			\$31.48	91%
Unweighted average, reference countries			\$29.70	89%

* For Switzerland, only 2013 per capita income was available.

One defense for the high U.S. price for Xtandi would be that the product could not have been developed at a lower price. But given the significant market for this drug, the federal subsidies in both the preclinical and clinical stages, and the fact that prostate cancer is the among the three most common types of cancer,⁵² that defense can be rejected entirely, and certainly going forward, given the billions of dollars in revenue already earned by Astellas.

16. Conclusion

We are requesting the federal government take steps to address the discriminatory and unfair pricing of Xtandi/enzalutamide by Astellas. U.S. residents should not have to pay two to four

⁵² American Cancer Society: Cancer Facts and Figures 2015. Atlanta, Ga: American Cancer Society, 2015.

times as much for a cancer drug than residents of other high income countries, particularly when the drug was invented with the support of federal grants and benefited from other federal research subsidies. The average wholesale price for Xtandi was \$129,269 per year in 2015, and this was more than twice as high as the price in any other high income country in our 13 country survey, and four times as high as the price in Canada. U.S. taxpayers are generous when it comes to financing research programs at the NIH, the U.S. Department of Defense, and in other federal agencies. However, we should not allow the companies that commercialize this research to discriminate and use unfair prices that impose financial hardships on U.S. residents, create access barriers for cancer patients, and make our workforce less competitive in global markets.

There are many areas where current U.S. laws are inadequate to address excessive or unfair prices. This is not one of them. The Bayh-Dole Act was passed with the promise that the federal March-In rights or the federal government royalty-free rights in patents would be available to protect the public from the unreasonable use of patented inventions. This is such a case.

Please contact Andrew S. Goldman, counsel for Policy and Legal Affairs at KEI, about this request. He can be reached at andrew.goldman@keionline.org, or by telephone at +1.202.332.2670.

Sincerely,

James Packard Love, Andrew S. Goldman, Diane Singhroy, Zack Struver, Claire Cassedy and Elizabeth Rajasingh, on behalf of
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Washington, DC 20009
<http://keionline.org>

Manon Ress, Michael Davis and Ruth Lopert, on behalf of
Union for Affordable Cancer Treatment (UACT
<http://cancerunion.org>

Cc:

Army research Laboratory
Domestic Technology Transfer (Patent Licensing, Cooperative R&D Agreements, Test Service Agreements) via ORTA@arl.army.mil

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Senators Boxer, Brown, Grassley, King Leahy, McCain McCaskill Nelson Sanders, Schumer
Sessions, and Wyden

Representatives Doggett, Schakowsky, Tom Price, Markwayne Mullin, the Congressional
Prostate Cancer Task Force

From: Knezevic, Vlado (NIH/NIDDK) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=3CD7FD096830401C88A2C03EC1916B3C-KNEZEVICV2]
Sent: 5/13/2020 2:50:23 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Knezevic, Vlado (NIH/NIDDK) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3cd7fd096830401c88a2c03ec1916b3c-knezevicv2]; Niebylski, Charles (NIH/NIDDK) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3248b0e1497e439b94ce47c2f52b0268-niebylskicd]
Subject: RE: Draft Response to KEI Objection
Attachments: 2a_KEI Comments re License for Exendin-4 Gene Transfer to Kriya Therapeutics, Inc. (1).pdf; 2b_Response to KEI Comments re License for Exendin-4 Gene Transfer to Kriya Therapeutics, Inc._ver13May2020.docx

Hello Mark – per your request, attached is proposed response (in Word – PDF document was received from them). Any additional guidance would be appreciated!
Best,

Vlado

Vladimir Knezevic, MD

Senior Advisor for Commercial Evaluation

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, April 28, 2020 6:00 PM
To: Knezevic, Vlado (NIH/NIDDK) [E] <vlado.knezevic@nih.gov>
Cc: Niebylski, Charles (NIH/NIDDK) [E] <charles.niebylski@nih.gov>
Subject: FW: Draft Response to KEI Objection

Vlado:

Here is a draft response from earlier this week from NCI. It gives you an idea of how we usually respond. Taylor it to their letter in your own words, and run it by me please.
The date of my letter to them (a blank in the edits) was Nov 26, 2019
Thanks,

REL0000024906

Mark



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April 28, 2020

Vladimir Knezevic, MD
Senior Advisor for Commercial Evaluation
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Building 12A, Room 3011
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Via Email: vlado.knezevic@nih.gov

Re: Prospective Grant of an Exclusive Patent License: AAV Mediated Exendin-4 Gene Transfer to Salivary Glands To Protect Subjects From Diabetes or Obesity

Dear Dr. Knezevic:

Knowledge Ecology International (KEI) and James Love are writing to comment on the “Prospective Grant of an Exclusive Patent License: AAV Mediated Exendin-4 Gene Transfer to Salivary Glands To Protect Subjects From Diabetes or Obesity” to Kriya Therapeutics, Inc.¹

The invention covered by the license, which was successful in preclinical studies, could help regulate blood sugar in patients with diabetes and promote weight loss in individuals suffering from obesity—conditions affecting large numbers of Americans and hundreds of millions of people worldwide.

The National Institutes of Health (NIH) may not execute the license unless it considers all timely-submitted public comments and concludes that the criteria listed at 35 U.S.C. § 209(a) are satisfied. The NIH did not answer the majority of the questions KEI asked about the license, limiting our ability to comment on it.

From what KEI can tell, the license does not satisfy the criteria located at 35 U.S.C. § 209(a), because the NIH apparently has not engaged in an individualized assessment to determine whether exclusivity is a reasonable and necessary incentive, nor has it limited the proposed scope of exclusivity to not broader than the necessary incentive.

¹ 85 Fed. Reg. 20508, available at <https://www.federalregister.gov/documents/2020/04/13/2020-07706/prospective-grant-of-an-exclusive-patent-license-aav-mediated-exendin-4-gene-transfer-to-salivary>.

Because the license disposes of government-owned property, the NIH may not grant it unless the NIH first requests the antitrust advice of the U.S. Attorney General, which it apparently has not done.

If the NIH grants the license, we request that it incorporates a series of provisions designed to safeguard the public interest in the invention, promote the policy objectives of the Bayh-Dole Act, and implement the policies outlined in the Public Health Service (PHS) Technology Transfer Manual.

Background

The proposed license covers an invention involving the use of an adeno-associated viral vector to deliver exendin-4 to the salivary gland as a treatment for diabetes and obesity.

The abstract for the invention at the NIH Office of Technology Transfer website states that the invention “resulted in improved glucose homeostasis and weight profile in two rat models of obesity and type 2 diabetes.”²

The prospective licensee, Kriya Therapeutics, Inc., is incorporated in Delaware and registered to conduct business in California. Kriya Therapeutics’ website contains little information apart from a two-paragraph description of the company and short biographies of its executive officers. The website does not list which, if any, products are in Kriya Therapeutics’ pipeline, but states that the company’s mission is “to expand the reach of gene therapy to address highly prevalent diseases affecting millions of patients.”³ This is consistent with a company that applied for a license to a potential treatment for diabetes and obesity.

Discussion

As explained in greater detail below, KEI notes the following points about the proposed license:

1. The NIH was not transparent about the license, limiting our ability to comment on it, a right provided to the public by 35 U.S.C. § 209(e);
2. The license does not satisfy the criteria located at 35 U.S.C. § 209(a), because the NIH apparently has not engaged in an individualized assessment to determine whether exclusivity is a reasonable and necessary incentive, nor has it limited the proposed scope of exclusivity to not broader than the necessary incentive;
3. The NIH apparently has not sought the antitrust advice of the U.S. Attorney General regarding the license, as required by 40 U.S.C. § 559; and

² <https://www.ott.nih.gov/technology/e-142-2011>.

³ <https://web.archive.org/save/https://kriyatherapeutics.com/>.

4. If the NIH proceeds with the license, we recommend that it includes a series of provisions designed to safeguard the public interest and ensure that the license implements the governing principles listed in the PHS Technology Transfer Manual.

1. The NIH was not transparent about the license, limiting our ability to comment on it, a right provided to the public by 35 U.S.C. § 209(e).

A federal agency may not grant an exclusive license to government-owned technology without first notifying the public of the prospective license, allowing a minimum 15-day period for the public to comment, and considering all timely-submitted comments. 35 U.S.C. § 209(e).

For the public to meaningfully comment on a proposed license, it must have basic information relevant to the license, and in particular, to the controlling issue—whether the license is authorized because it satisfies all of the criteria listed at 35 U.S.C. § 209(a).

On April 24, 2020, KEI emailed Dr. Vladimir Knezevic, the point of contact for the license, a list of eight questions. He answered only the first two questions, both of which concerned the development stage of the invention. In declining to answer the remaining questions, he stated that those questions either were irrelevant or had already been answered. Both assertions are incorrect.

Among the questions that Dr. Knezevic refused to answer were (1) how the NIH concluded that exclusivity is a necessary incentive and (2) how it concluded that the scope of exclusivity is not broader than necessary. These are two of the requirements that the NIH must satisfy before it may grant an exclusive license. By failing to answer questions that relate to whether the proposed license satisfies 35 U.S.C. § 209, the NIH withheld information that is directly relevant to the issue at hand.

Nor had the NIH ever answered the questions that Dr. Knezevic refused to answer. The questions that KEI emailed Dr. Knezevic were unique to the instant patent license, and April 24, 2020 was the first and only time KEI asked about this license.

The Bayh-Dole Act gives the public a role in licensing decisions concerning inventions that are owned by the public. Because the questions KEI asked and Dr. Knezevic failed to answer were relevant and had not previously been answered, Dr. Knezevic had no basis for not answering them. The NIH's lack of transparency undermined KEI's ability to comment on the license.

2. The NIH apparently has not meaningfully applied the criteria for granting an exclusive license.

The NIH may not license a federally-owned invention on an exclusive or partially-exclusive basis unless, among other criteria:

(1) “granting the license is a reasonable and necessary incentive to -- (A) call forth the investment capital and expenditures needed to bring the invention to practical application; or (B) otherwise promote the invention’s utilization by the public;” and

(2) “the [NIH] finds that the public will be served by the granting of the license . . . and that the proposed scope of exclusivity is not greater than reasonably necessary[.]”

35 U.S.C. § 209(a)(1)-(2).

As noted previously, KEI asked Dr. Knezevic how he evaluated the above-listed criteria to determine that an exclusive license is a reasonable and necessary incentive, and that “the proposed scope of exclusivity is not greater than reasonably necessary,” tracking the language of 35 U.S.C. § 209(a)(1)-(2).

In declining to answer those questions, Dr. Knezevic stated that they had already been answered. While that statement is inaccurate, his response is consistent with past statements by NIH technology transfer officials, who employ across-the-board assumptions for exclusive patent licenses. For example, Dr. Mark Rohrbaugh, Special Advisor for Technology Transfer to the NIH Deputy Director for Intramural Research, stated in a letter to KEI that the NIH “works in a market for these early-stage therapeutic technologies in which there is essentially no demand for nonexclusive licenses” and that “companies and investors . . . require an exclusive license for the full patent term.” In relation to a previous proposed exclusive patent license, an NIH technology transfer officer stated: “I do not personally have any licenses on my docket granted for a term shorter than the full patent term and am unaware of any that may have been granted by my colleagues at other Institutes.”

(For clarity, KEI notes that the NIH has been requested to limit the term of exclusivity of the license, not the term of the license.)

Dr. Knezevic’s reference to past NIH statements about unrelated licensing decisions indicates that the answers to KEI’s unanswered questions are as follows:

- The NIH is proposing an exclusive license because it assumes that no company will commit to licensing the technology without full exclusivity; and
- The NIH is proposing to grant the broadest possible rights to the technology because it assumes that no company will commit to licensing the technology without the broadest scope of exclusivity.

Because each license presents unique technologies and circumstances, such a one-size-fits-all approach is not consistent with the Bayh-Dole Act. Where it is possible to limit rights to an invention, the agency proposing to grant an exclusive or partially exclusive license must do so.

The subject technology has performed well in preclinical studies—the riskiest stage of development—and the preclinical research was funded by the public sector.⁴ If successful, the technology will have a huge market size, considering the prevalence of diabetes and obesity. In 2018, 34.2 million Americans, or 10.5 percent of the population, had diabetes.⁵ According to the Centers for Disease Control and Prevention, in the United States, “[t]he prevalence of obesity was 42.4 percent in 2017~2018.”⁶ In addition, this is a worldwide license. According to the World Health Organization (WHO), in 2014, the global prevalence of diabetes among adults over 18 years of age was estimated at 8.5 percent of the world population.⁷ The WHO also estimated there were more than 300 obese adults in 2000.⁸

Given the potential value of the technology and the requirement to limit the scope of the license, it is concerning that the proposed scope of the license has not been limited in any discernible way.

Considering the NIH’s previous gene therapy licensing practices, we can safely assume that the period of exclusivity for this license is life-of-patent—the broadest possible duration.

The proposed territorial reach for the license is also as broad as possible—worldwide.

Likewise, the proposed field of use is as wide as possible. While the NIH will not concede that it is required to limit the duration of an exclusive patent license, it does acknowledge that it is required to limit the field of use for such licenses. Here, however, the field of use apparently embraces all potential commercial applications for the subject invention: “prevention and treatment of type-2 diabetes and obesity.”⁹

If, in fact, the NIH has not considered whether a non-exclusive or partially-exclusive license is possible, and it has not explored whether it could narrow the duration of the license, territorial reach, or field of use—perhaps to either diabetes or obesity, but not both indications—it has not satisfied 35 U.S.C. § 209(a)(1)-(2).

⁴ Di Pasquale, Giovanni et al. “Sustained exendin-4 secretion through gene therapy targeting salivary glands in two different rodent models of obesity/type 2 diabetes.” PLoS one vol. 7,7 (2012): e40074. doi:10.1371/journal.pone.0040074.

⁵ <https://www.diabetes.org/resources/statistics/statistics-about-diabetes>.

⁶ <https://www.cdc.gov/obesity/data/adult.html>.

⁷ <https://www.who.int/news-room/fact-sheets/detail/diabetes>.

⁸ <https://www.who.int/nutrition/topics/obesity/en/>.

⁹

<https://www.federalregister.gov/documents/2020/04/13/2020-07706/prospective-grant-of-an-exclusive-patent-license-aav-mediated-exendin-4-gene-transfer-to-salivary>. According to the invention abstract, the potential commercial application for the invention is “[t]herapy for diabetes or obesity.” <https://www.ott.nih.gov/technology/e-142-2011>.

3. The NIH apparently has not sought the antitrust advice of the U.S. Attorney General regarding the license, as required by 40 U.S.C. § 559.

We object to the license because the NIH has not first obtained the antitrust advice of the United States Attorney General.

Under the Federal Property and Administrative Services Act, 40 U.S.C. § 101 *et seq.*, “[a]n executive agency shall not dispose of property to a private interest until the agency has received the advice of the Attorney General on whether the disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law.” 40 U.S.C. § 559(b)(1).

This includes when the NIH proposes to grant an exclusive license in federally-owned technology. “Property” is defined at 40 U.S.C. § 102 to mean “any interest in property.” The statute exempts personal property if the fair market value is less than \$3,000,000, but specifically excludes “a patent, process, technique, or invention” from that exception.

The regulation 41 C.F.R. § 102-75.270 also makes clear the inclusion of patents “irrespective of cost.”

KEI asked Dr. Knezevic whether the NIH requested the advice of the U.S. Attorney General concerning the licenses. Dr. Knezevic did not answer. In the past, the NIH has asserted its position with respect to 40 U.S.C. § 559 as follows:

The statute you reference is directed to the disposal (assignment) of government property. It has little relevance to our patent licensing activities, which are principally governed by the Bayh-Dole Act and its regulations.

We disagree.

35 U.S.C. § 209(a)(4) allows a federal agency to grant an exclusive license only if the license “will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws.” 35 U.S.C. § 211 provides that “[n]othing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law[.]” The Bayh-Dole Act sets out the areas in which the statute “shall take precedence over any other Act which would require a disposition of rights in subject inventions[.]” 35 U.S.C. § 210, and mentions 21 separate statutes, but not the FPASA.

The term “disposal” is not a defined term under 40 U.S.C. § 102 of the FPASA, and is not limited to “assignment” or “sale.” In fact, there are many examples of regulations and laws that include licensing amongst dispositions, either explicitly or by implication.

If NIH grants an exclusive license in a federally-owned invention, it is disposing of a government property interest so as to trigger 40 U.S.C. § 559.

4. In the event that the NIH decides to grant the license over our objections, we recommend that the NIH includes a series of provisions designed to safeguard the public interest and ensure that the license implements the principles listed in the Public Health Service (PHS) Technology Transfer Manual.

In the event that the NIH proceeds with the license, KEI requests that it includes the following provisions to protect the public's interest in the NIH-funded technology:

1. **Geographic Scope of Exclusivity.** If the NIH decides to grant exclusive rights to the subject invention, it should limit exclusivity to any country with at least 35 percent of the per capita income of the United States, but not the United States, so that high income countries that did not fund the R&D underlying the invention would bear the costs of the exclusivity, while U.S. residents would not. The NIH should license the invention on a non-exclusive basis in countries with per capita incomes less than 35 percent of the United States. For countries of moderate or low income, the monopoly is likely to have an adverse impact on access with fewer benefits in terms of the incentives for investors.
1. **Price discrimination.** In the event that exclusivity is extended to the United States, any medical technology using the patented invention should be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method. This is a modest safeguard.
2. **Low and middle income countries.** As noted, the exclusive license should not extend to countries with a per capita income less than 35 percent of that of the United States, in order to ensure that the patents do not lead to restricted and unequal access. If the NIH rejects this suggestion, it needs to provide something that will give effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."
3. **Global registration and affordability.** The license should require Kriya Therapeutics to disclose the steps it will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the WHO, either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.

4. **Medicines Patent Pool.** The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the medical technology from competitive suppliers, including technology transfer, in any country where there is a finding by the Department of Health and Human Services (HHS) or the WHO that people in these markets do not have sufficient access to the medical technology.
5. **Years of exclusivity.** We propose the license reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddl case. We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the invention exceed certain benchmarks. For example, the period of exclusivity in the license could be reduced by one year for every \$500 million in global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 U.S.C. § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”
6. **Transparency of R&D outlays.** Kriya Therapeutics should be required to file an annual report to the NIH, available to the public, on the R&D costs associated with the development of any product or service that uses the invention, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward, the company be required to report on actual R&D outlays to develop the subject invention. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, including that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.” Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk-adjusted costs of bringing NIH-licensed inventions to practical application.

Conclusion

The NIH’s failure to answer KEI’s questions about this license has undermined our ability to comment on it, a right that is protected by 35 U.S.C. § 209(e). The NIH may not execute the license unless it fulfills all criteria listed at 35 U.S.C. § 209(a), and blanket assumptions may not replace the necessary individualized assessment. Because the license disposes of government-owned property, the NIH may not grant the license unless it first requests the antitrust advice of the U.S. Attorney General. 40 U.S.C. § 559. In the event that the NIH grants the license, we ask that it incorporates the provisions listed above, which are designed to

protect the public interest in the licensed technologies and to accomplish the policies outlined in the PHS Technology Transfer Manual.

Sincerely,

1. Knowledge Ecology International
2. James Love (in his individual capacity)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health/ NIDDK
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b5

Sincerely,

Vlado Knezevic, M.D.
Senior Advisor for Commercial Evaluation

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 1/13/2020 10:41:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder

Note that Misha

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From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Monday, January 13, 2020 4:14 PM
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Goldstein, Bruce (NIH/NHLBI) [E] <goldsteb@mail.nih.gov>
Subject: RE: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder

I suggest

b5

You might then

b5

b5

You could

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I think it would be good

b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Sent: Sunday, January 12, 2020 10:23 AM
To: Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Goldstein, Bruce (NIH/NHLBI) [E] <goldsteb@mail.nih.gov>
Subject: FW: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder

Mark, Dale, and Bruce—KEI's comments regarding our FR notice for OcQuila enclosed and my proposed response. Please comment.
I'd appreciate feedback before next Friday as I'd like to send a response letter back to them COB Jan 17, 2020.

Thanks!

Michael A. Shmilovich, Esq., CLP



National Heart, Lung,
and Blood Institute

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From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
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To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: Comments, Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder

Dear Mr. Shmilovich:

Attached, please find KEI's comments regarding "Prospective Grant of an Exclusive Patent License: Gene Therapy for Ocular Disorder" (84 FR 65169) and the relevant attachments.

Thank you,

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